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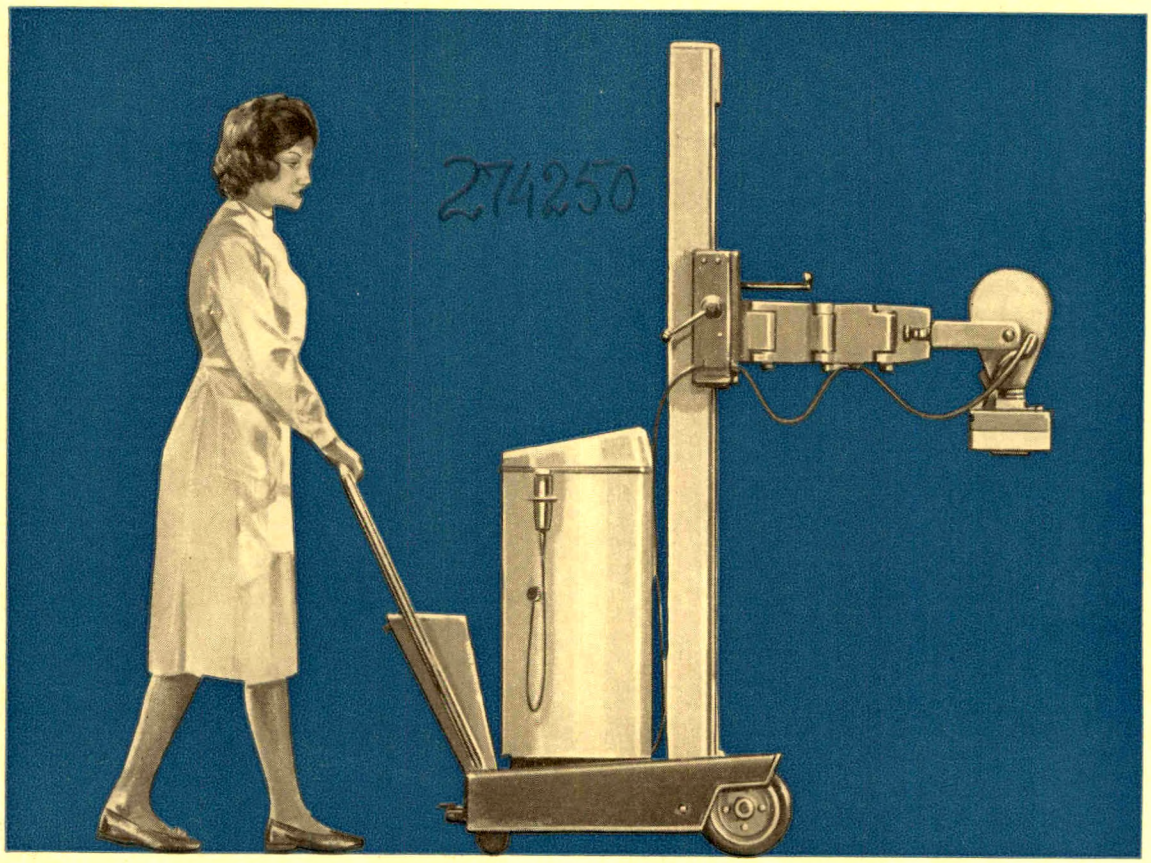


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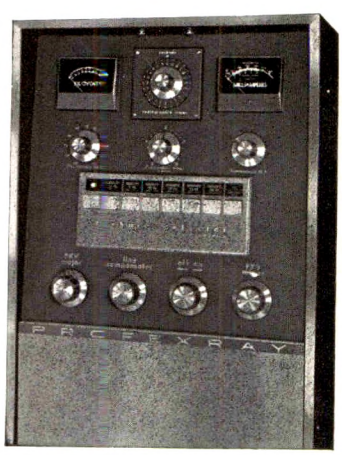
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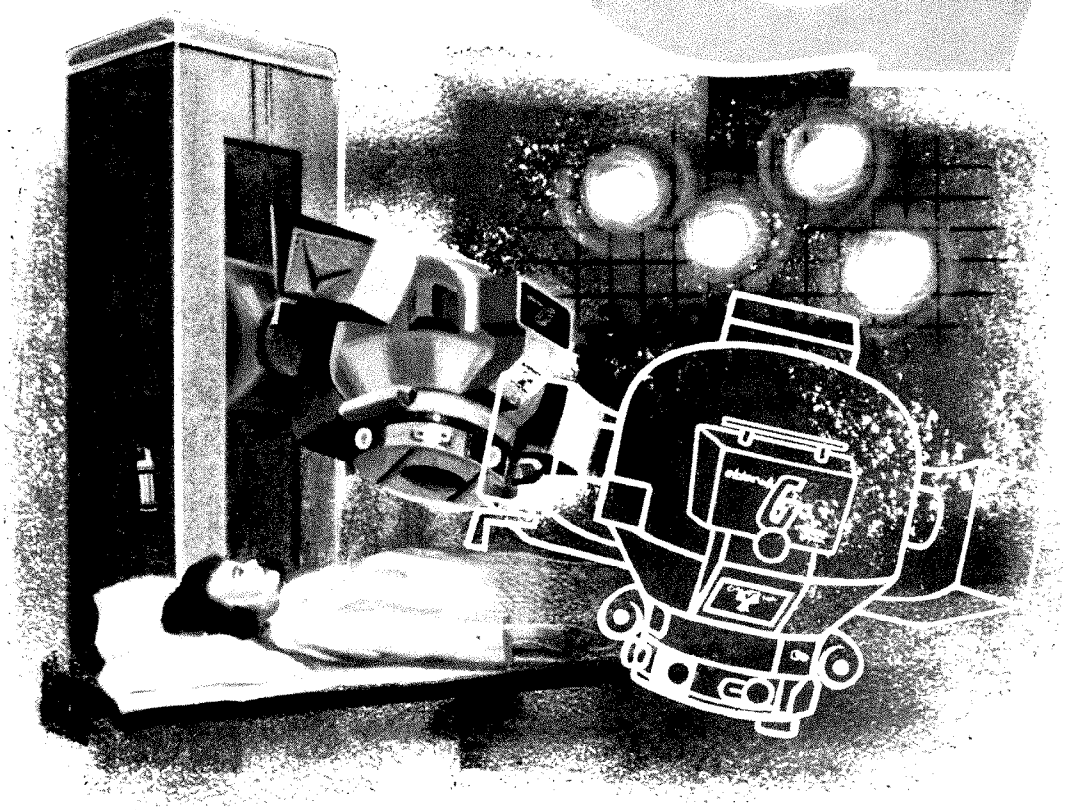
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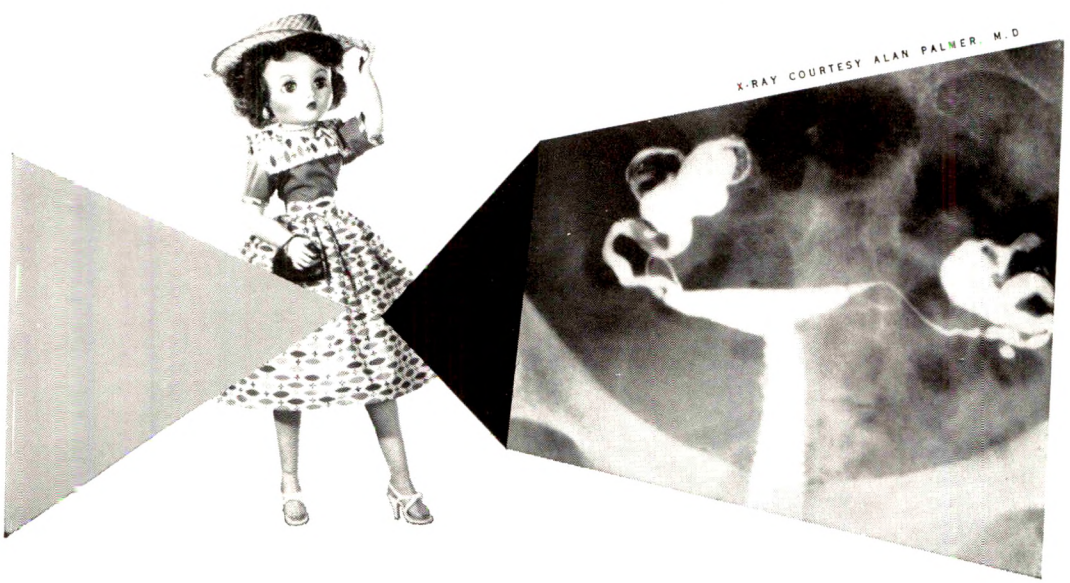
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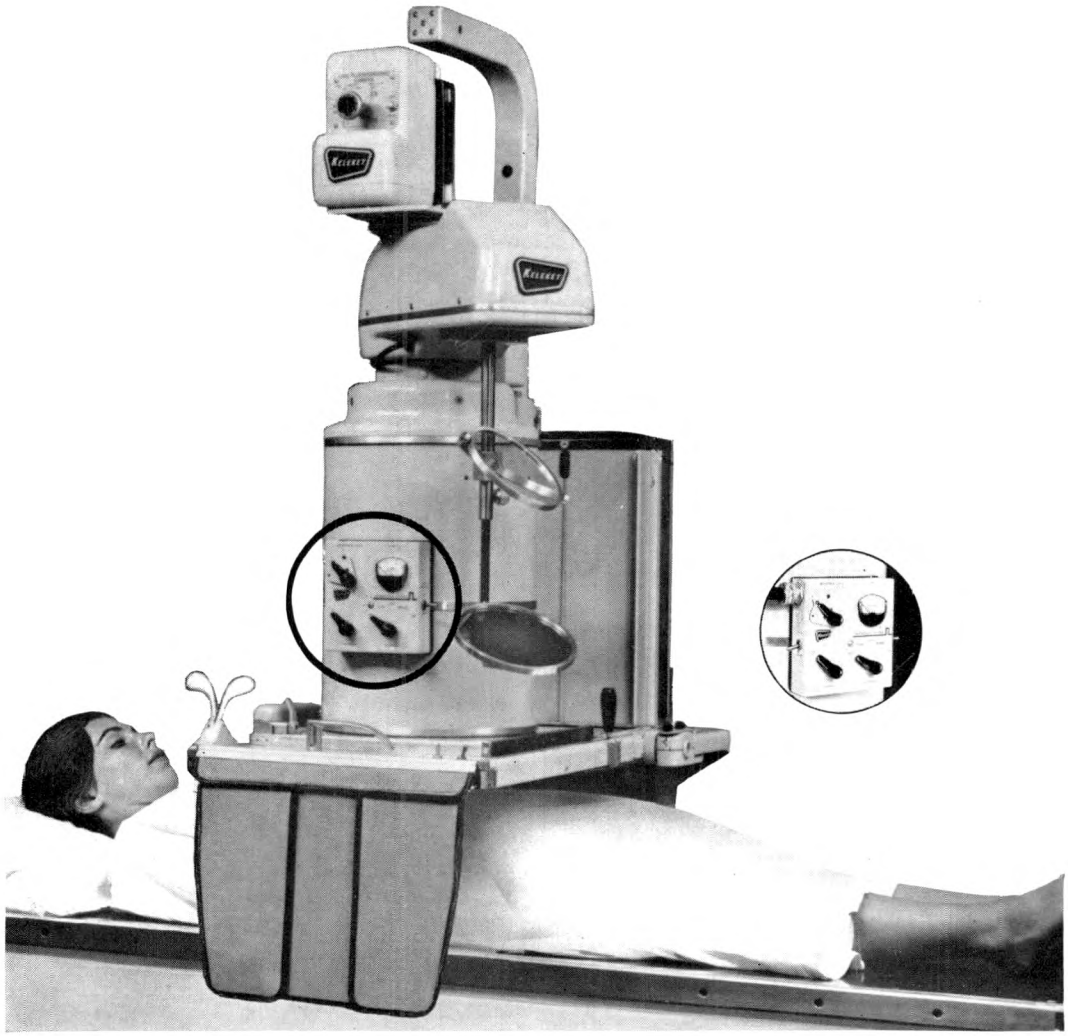
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RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 86 OCTOBER, 1961 No. 4

RADIATION THERAPY OF CANCER*

CURRENT RESULTS WITH MEGAVOLTAGE AND ORTHOVOLTAGE

By L. HENRY GARLAND, M.B., M.D.†
SAN FRANCISCO, CALIFORNIA

RADIATION therapy, skilfully employed, continues to be a prime weapon for the cure and palliation of certain types of cancer. For localized cancer of sites such as skin, lip, oral cavity, eyelid and larynx, it provides cure rates equal to or better than those obtainable by radical surgery, and with *superior functional* results;[12] for cancer of the cervix it provides in general *better cure rates* than does surgery, with lower morbidity and mortality;[10] for lymphoblastoma and chronic leukemia it provides somewhat safer treatment than chemotherapy, with *less morbidity*.[12] For certain tumors no longer localized, such as seminoma testis and medulloblastoma cerebelli, it provides a goodly percentage of five year arrests. For selected cases of breast and endometrial cancer, it also provides long term control.

One of the questions facing the physician attending a patient with cancer (and certain other diseases suitable for radiation therapy) is: "Should I recommend supervoltage—or telecobalt—therapy?" That is, "Will megavoltage be better for my patient?" While this decision is normally best left to the treating radiologist, there are circumstances under which the patient expects the attending or family doctor to speak out. The purpose of this paper is to set forth certain facts in order to help him answer the question.

DEFINITIONS

Supervoltage therapy devices include roentgen-ray units operating in the 800 kv. to 2,000 kv. range, and for all practical purposes radioactive cobalt and cesium teletherapy units. The former have been in use for some thirty-two years, and cobalt 60 teletherapy units for about twelve years. Many radiologists use the term *megavoltage* for these devices, in order to avoid the tenuous connotation of the prefix "super." The *biologic* (cancericidal) effect of supervoltage radiation as ordinarily measured, is actually "infra" or inferior to that ob-

* From the Department of Radiology, San Francisco General Hospital, University of California Service (and formerly, the Stanford University Service), and the author's private practice.
Presented in part at the Cancer Conference of the American Society of Oral Surgeons, Phoenix, October 10–12, 1960.
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tainable with rays in the 250 kv. range.[10]

The so-called *effective* voltage of many roentgen-ray beams is considerably lower than the *peak* voltage, and is a better clue to their relative penetrating power. The latter is also recorded in terms of the thickness of a standard material, such as copper, which will reduce the transmitted radiation beam by a factor of one half (the HVL or half value layer equivalent factor). This may be recorded in other materials such as water, aluminum or lead, but for convenience of ready comparison the half value layer in copper of several different radiation beams is listed in Table 1.

The term *orthovoltage* deep therapy is applied to 200–400 kvp. roentgen-ray beams, the equivalent effective voltage of which is from 0.07 to 0.12 million electron volts or mev.*

The term *megavoltage* deep therapy, or supervoltage, is applied to conventional roentgen-ray beams in the 1,000 kvp.–15,000 kvp. range, that is, one to fifteen million volts; the real or effective voltages of these beams range from 0.5 to 5 mev. The beams may be from linear accelerators and other sources. Iridium 192, cesium 137, cobalt 60 and radium teletherapy units yield hard roentgen rays or gamma rays in or close to this effective voltage range (see Table 1).

The term *ultra-high voltage* deep therapy is employed for betatrons (in the 10–50 mvp. range), synchrotrons and similar high energy devices used to produce hard roentgen rays as well as electron beams and so forth. Neutron, proton and certain other beams may be included in this category.

The radiologist also has available low voltage roentgen-ray beams (50 kvp.–150 kvp.), as well as beta and alpha "ray" beams derived from natural or artificial radioactive materials.

There are many devices for applying, aiming or modifying *external* radiation beams, including equipment for: *fixed beams; moving beams* (rotation, arc, spiral, pendulum and traveling beams); and *re-*

* The Joint Commission of the International Atomic Energy Agency and the World Health Organization meeting in Vienna, August, 1959 defined orthovoltage as being in the 200–400 kv. range.

TABLE I

SOME EXTERNAL RADIATION SOURCES

Term	Source (usually peak voltage)	Approximate mev. Equivalent	HVL mm. Cu*	Relative Biologic Equivalent
Orthovoltage deep therapy	250 kv. roentgen ray	.1	1–3	1
Megavoltage deep therapy	1,000 kv. roentgen ray	.5	8	.75–.85
	Cs^{137} teletherapy	.6	8	
	Radium teletherapy	.8	13	
	Co^{60} teletherapy	1.2	14	
	"6 million" volt linear accelerator	1.6	15	
Ultra-high voltage therapy	23 mv. roentgen ray	8	"32"	1.75
	70 mv. roentgen ray	23	"33"	

* Copper is used in this table to permit ready comparisons; in ordinary practice lead is used above 1,000 kv.

stricted beams (grid-therapy and wedge filter therapy).

With these devices radiations may be circumscribed, "pinpointed," "aimed," "localized" and otherwise applied with varying degrees of precision. Roentgen or gamma rays cannot, of course, be focused.

Radiations may be applied internally via: intracavitary cones or cylinders; interstitial tubes, needles, seeds, threads, colloidal suspensions and solutions; intravascular injections; and intracavitary instillations.

Basic principles of effective radiation therapy of cancer may be defined as follows:

1. Determination of the *histologic type* and estimation of the *anatomic extent* (*or stage*) *of the tumor.*

2. Determination of the *clinical status of the patient;* some patients with cancer may be too ill from other disorders to warrant radical therapy of the neoplasm.

3. Selection of the *treatment modality* apt to result in the least physical and economic trauma; this modality may be orthovoltage, megavoltage, cobalt 60, radium or other means.

4. *Meticulous planning and application* of irradiation, with deliverance of an optimum dose to the tissue of interest.

5. Provision for necessary associated medical and surgical treatment.

6. Conscientious *after care and follow-up.*

Radiosensitivity constitutes responsiveness to radiation in terms of tumor cell destruction, but with regeneration and recuperation of adjacent normal cells. It is a complex phenomenon, depending on many factors such as tumor cell type, tumor size, blood supply, infection, anatomic location and other factors. *It cannot be predicted from the microscopic appearance* and is not synonymous with radiocurability. Many localized squamous cell tumors are relatively insensitive (requiring large doses of radiation for cure), but *are* quite radiocurable. Conversely, some lymphomatous tumors are very radiosensitive, but are seldom curable. *Radiocurability* depends on factors such as the tumor cell type, the size of the tumor, its anatomic extent, the tolerance of adjacent structures, the degree of natural drainage and so forth. A localized adenocarcinoma of the cervix uteri is usually radiocurable; a lymphosarcoma of the tonsil, with mediastinal lymph node spread usually is not.

A curative dose for localized carcinoma is defined as that dose which is destructive of tumor cells without irreparable injury to adjacent normal cells. For many squamous cell tumors it ranges from 4,500–5,500 orthovoltage rads, to limited areas (*e.g.*, 5×5 cm.), delivered in about four weeks time—*or the equivalent in dose and time.* Such cancericidal dose-time equivalents, when fairly even fractionation is used, include: about 2,000 rads in one day; 4,000 rads in eight days; and 6,000 rads in thirty-two treatment days.

The main reason for fractionation and protraction of dose is to aid normal tissue recovery; this applies especially to structures such as bone and cartilage.

Dosage alone is not the decisive factor in clinical cure of many localized cancers; histologic and biologic factors are more important. Glücksmann and Cherry[14] in a study of 615 cases of cervix cancer found the optimal range to be from 6,000–7,000 combined orthovoltage and gamma r in the paracervical tissues at point A. For Stages I and II the greatest five year survival rate was found in the lowest dose range.

INDICATIONS FOR DIFFERENT VOLTAGES

The radiologist is concerned with the deliverance of an adequate dose of ionizing radiation to the tissue of interest, with maximum possible safety to adjacent normal structures. The dose may be delivered by widely different beams and devices, depending on the equipment at hand, the skill and experience of the therapist, the location of the tumor, the status of the overlying or adjacent tissues, and other matters.

In general, most superficial lesions (skin or lip) can be effectively treated with "low voltage" roentgen-ray units operating at

50–150 kvp. When such lesions infiltrate deeply (*e.g.*, extensive skin carcinoma of the inner canthus region), they are no longer superficial and more penetrating radiation will tend to result in more homogeneous ionization of the tumor. Still deeper lesions can be effectively treated with "orthovoltage" units in most instances—combined with intracavitary or interstitial radium or radioactive cobalt in selected sites such as uterus, tongue and maxillary antrum. With these units one can readily deliver more radiation than the normal deep structures will tolerate. Simon and Silverstone[37] write: "The increase in depth dose with cobalt 60 teletherapy is too often considered to be the major advantage of this form of therapy, although there are no deep seated lesions which cannot receive a cancericidal dose with 200 kv. radiation with multiple fields. . . . We are limited in dosage of deep seated lesions by the radiosensitivity of adjacent organs, not by the lack of penetrability of our rays."

Then why megavoltage? Because in selected cases such as very thick or obese persons, or rare circumscribed tumors unsuited for radical surgery such as retinoblastoma in a remaining eye, the physical property of the harder beam may permit more effective irradiation. Also in persons with tumors situated beneath skin badly damaged by prior disease or injury, the initial skin-sparing effect of megavoltage will usually permit more effective treatment.

When delivered with megavoltage beams, a larger physical dose must be used for a given biologic effect. The factor varies and is indicated by approximate figures in Table 1. In general, and with all other technical factors (such as distance, field size, fractionation and associated matters) remaining the same, one needs from 20 to 30 per cent more administered physical dose in megavoltage rads to equate a given biologic effect of orthovoltage rads. This fact, though known for several decades, is often not appreciated.[10] When it is, increase in radiation comfort with megavoltage often proves evanescent.

ADVANTAGES OF MEGAVOLTAGE

The relative advantages of megavoltage have been described under the following headings: 1. Increased depth dose. 2. Diminished skin dose. 3. Decreased bone dose. 4. Greater patient comfort. 5. Better results.

1. *Increased Depth Dose.* This is more correctly expressed as "increased *physical* depth dose." When allowance is made for the decreased biologic efficiency of megavoltage beams, it is found that for many *clinical* situations the biologically effective depth base is little greater than with orthovoltage.

Opposing fixed beams provide the most accurate way of "cross firing" or dosing deep-seated tumors. When nonopposing or oblique fields are used, the tumor may be incorrectly centered and therefore partly underdosed. When rotation therapy is used, the volume usually requiring treatment tends to result in undesirable general reactions, except in selected cases of cancer of the esophagus—and even in this site, the clinical results of rotation therapy leave much to be desired.

Opposing fields present a limitation for megavoltage beams because of the increased dose at the far side of the patient (the exit dose). This automatically limits the amount that can be given to each field with safety, and tends to offset the advantage of increased penetration. The matter is illustrated by considering a small mid-pelvic tumor which is to be treated in conjunction with intracavitary radium (Fig. 1). Let us assume an average patient of 20 cm. thickness. Since megavoltage (in this case telecobalt) produces maximum ionization beneath the skin, and orthovoltage does so in the skin itself, these two zones require separate consideration as far as tolerance is concerned. Let us assume conventional orthovoltage factors of 200 kvp., HVL 1 mm. copper, target-skin distance of 80 cm., and

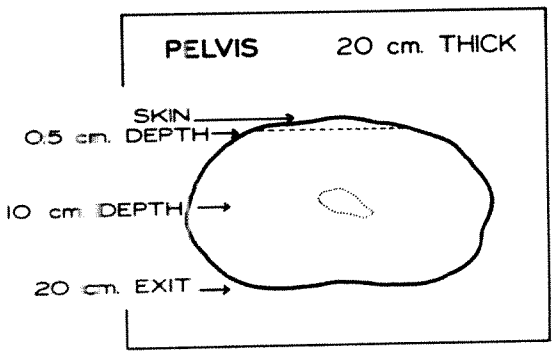


FIG. 1. Diagram of cross section of pelvis, with dotted outline of theoretical tumor in mid-portion.

field size 10×10 cm; the telecobalt factors include HVL 14 mm. copper, source-skin distance of 50 cm., and field size 10×10 cm. The diagrams (Fig. 2 to 4) show that with two opposing beams one needs with megavoltage a smaller skin dose, but *a higher subcutaneous tissue dose* to deliver biologically equivalent doses of radiation to the midpelvis. The 10×10 cm. field size is used so as to give the advantage to megavoltage. The relative improvement in midplane depth dose with megavoltage is about 65 per cent with 10×10 cm. beams, but only about 25 per cent with 20×20 cm. fields. The latter are often necessary in clinical cancer treatment, and of course further decrease the comparative value of megavoltage.

The diagrams show that a subcutaneous dose of 5,000 mv. rads is reached under the conditions described. This dose, delivered in 4 weeks, is apt to be followed by *late* fibrosis and other undesirable reactions, which tend to offset the *early* gain of decreased skin reaction.

To avoid cross firing the same subcutaneous area, 3 nonopposing fixed beams, or a rotating beam, are often employed. The three nonopposed fields may be an anterior one and two oblique posterior fields; the rotation beam may consist of a 260 degree arc. Data from Chamberlain[3] show that

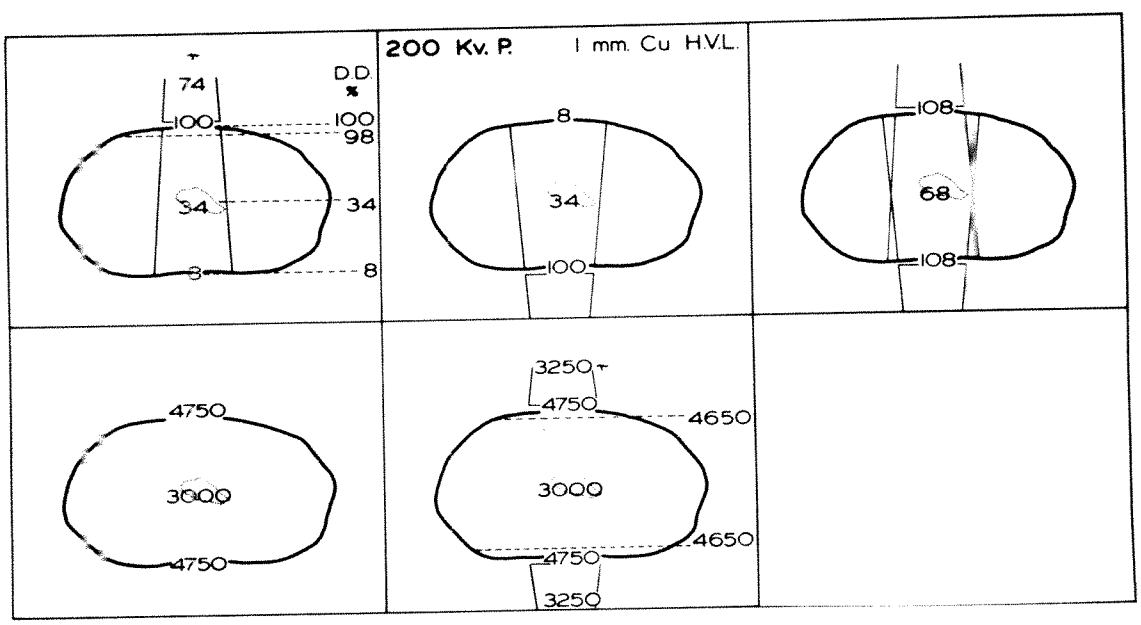


FIG. 2. Diagrams showing depth doses with orthovoltage therapy (200 kv.), half value layer 1 mm. copper 80 cm. target skin distance, field 10×10 cm., pelvis 20 cm. thick. Note that for 74 r delivered in air to an anterior field, there is a skin dose of approximately 100 r, a 10 cm. depth dose of 34 r, and an exit dose of 8 r. Accordingly, to deliver 3,000 r to a hypothetical tumor in the mid-pelvis via 2 opposing small fields of this type, one will deliver about 4,400 r to the skin of an anterior pelvic field and 4,400 r to the skin of a posterior pelvic field. With exit dose added, each skin field receives about 4,750 r. The approximate dose at 0.5 cm. beneath either of these fields is 4,560 r.

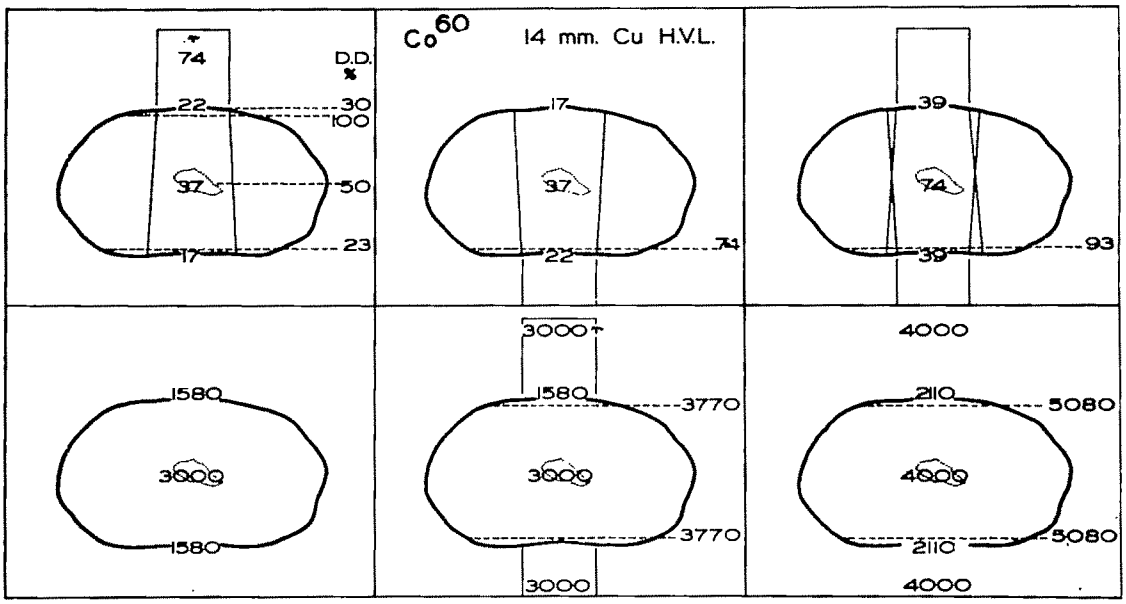


FIG. 3. Diagrams showing depth doses with 1,200 curie Co^{60} unit, half value layer 14 mm. copper, 50 cm. target skin distance, field 10×10 cm., pelvis 20 cm. thick. The skin dose is proportionately much less than that delivered with orthovoltage rays, but the subcutaneous tissue dose is slightly larger, if biologically equivalent doses are delivered to the mid-pelvis. The optimal low backscatter figure of 30 per cent is used; megavoltage beams of other types and size may result in 60 per cent skin dose.

either of these techniques does yield relatively improved *physical* depth dose with megavoltage. With megavoltage double arc rotation, the same tumor depth dose can be attained as with telecobalt rotation or three fields of 4 mev., *but there is a greater volume of nontumor tissue irradiated.* When allowance is made for the decreased biologic effectiveness of supervoltage radiation, the "250 kv. curve is appreciably close to the supervoltage ones." In other words, there is little or no significant increase in biologically effective depth dose with megavoltage under many ordinary clinical situations.

The shielding effect of bone with orthovoltage should and can be allowed for. With small beams (8×12 cm.) it can amount to about 20 per cent in the case of tissues underlying the sacrum or the thoracic spine. Conversely, the radiotransparency of the lung should be compensated for

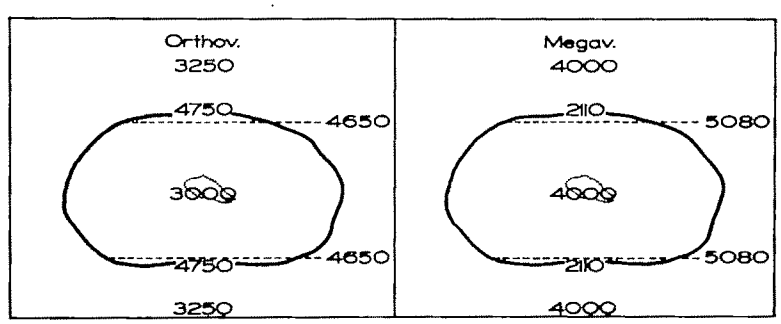


FIG. 4. Diagrams summarizing findings of Figures 2 and 3. The subcutaneous dose with cobalt 60 is actually larger than that with 200 kv. roentgen rays to attain biologically equal depth doses under the specific conditions described, that is 5,080 rads instead of 4,650 rads.

(it permits about 20 per cent more transmission than solid tissue). Neither physical feature limits effective orthovoltage therapy in clinical practice.

2. *Diminished Skin Dose.* This real property of megavoltage, often considered an advantage, is frequently the contrary. Skin erythema is a useful and readily visible indicator of, or clue to, deeper tissue tolerance. When there is a warning skin reaction, dosage can be reduced, protracted or terminated, and important deeper structures thereby protected. Serious and disabling late subcutaneous fibrosis, nerve damage, pulmonary fibrosis, gastrointestinal tract injury and perforation have been reported not infrequently following supervoltage therapy, despite an intervening relatively intact skin.

For persons of average build, skin tolerance is *not* the limiting factor in radiation therapy, but rather intestinal, bronchial and neural tissue tolerance.

Early skin reaction under radical radiation therapy will be more severe with orthovoltage, but late changes tend to be about equal—with subcutaneous injury added to the megavoltage dermal changes.[3,31]

3. *Decreased Bone Dose.* When physical measurements are made under laboratory conditions, the absorbed dose in *compact* bone is found to be about unity with megavoltage beams (as compared with a factor of 2 with orthovoltage). In other words 600 megavoltage r in compact bone yields about 600 megavolt rads, while 600 orthovoltage r yields about 1,200 rads. The physical dose in the adjoining *cancellous* bone and *bone marrow* is estimated as being about equivalent in terms of physical rads; the biologic dose is different by the previously mentioned factor of approximately 0.8. In *clinical* practice, Friedman *et al.*,[8] Schulz[28] and others[12,22] report that the incidence of bone necrosis with supervoltage therapy is similar to that from orthovoltage. Friedman *et al.* believe that "anatomic, clinical and pathologic factors contribute much more to the production of radionecrosis than the physical factors." Simon and Silverstone[37] report that "radionecrosis of the jaw has been observed after cobalt 60 and other forms of supervoltage irradiation, and may even increase in incidence because of our tendency to give larger doses when using supervoltage."

4. *Greater Patient Comfort.* Of all the intangibles in radiation therapy, this is one of the greatest. When large fields are employed and dosage is protracted in the manner often required in clinical cancer radiation therapy, it is usually found that there is as much nausea, vomiting, diarrhea and malaise with supervoltage as with orthovoltage therapy, when biologically equivalent doses are delivered. However, with small fields, and only physically equivalent doses, there is relatively less volume of tissue irradiated and less immediate skin reaction with supervoltage therapy; the smaller biologic dose naturally aids increased comfort, but results in inadequate therapeutic outcome.

We have seen many patients with decreased comfort following supervoltage treatment because of persistent neutropenia, late subcutaneous tissue damage, intestinal injury and bone necrosis. In general, megavoltage effects parallel orthovoltage reactions when equally large biologic doses are given.

By proper graduation of dose and suitable medical attention, patient comfort can be as readily assured with orthovoltage therapy as with megavoltage. When large fields must be used (*e.g.*, with ovarian carcinoma) patients may incur side effects with either voltage. In clinical practice, the virtue of the decreased volume or integral dose that occurs with megavoltage is seldom a major factor.

5. *Better Results.* There is no valid statistical evidence of improved cancer palliation or cure rates to date. Cancers of the uterus, esophagus and lung have not yielded better results with supervoltage therapy than with orthovoltage (Philips,[31] Buschke,[2] del Regato and Regaud,[6] Jacox,[16] Martin[23]). Even bladder cancer has proved disappointing (Friedman *et al.*,[9] Pointon[32]).

Comparative five year data will be found in the next section.

COMPARATIVE RESULTS

Valid comparison of results in cancer therapy is difficult because of differences in grading, staging and associated clinical care of two given groups of cases. However, when the two groups are from the same institution, of the same general type and stage, and cared for during a given decade by physicians of equal training and experience, comparison has some validity. Much of the following data is chosen for that reason.

A. HEAD AND NECK TUMORS

Larynx: Cantril[5] found no improvement in five year cure rates of larynx cancer with supervoltage therapy. His rates were 55 per cent with orthovoltage and 41 per cent with supervoltage therapy (20 and 36 cases, respectively). He noted that comparable series of patients treated at the University of California Hospital showed no difference—63 per cent five year arrests in each group (44 and 46 cases, respectively, in the orthovoltage and supervoltage groups). He wrote "one comes to the conclusion that in radiotherapy the quality of the radiologist and not that of the rays is the deciding factor . . . from evaluation of patients treated by others plus our own results, supervoltage roentgen rays or telecobalt would not appear to be an important factor."

Friedman, Southard and Ellett[8] write "For many lesions, supervoltage roentgen rays have been disappointing and it is probably preferable to use orthovoltage and interstitial radium." It is easy to irradiate the head and neck with supervoltage, but there is not an accompanying significant improvement in the arrest rate of such cancers. Indeed, "our previous experience with 250 kv. roentgen rays in the treatment of parotid cancers has been more favorable than with supervoltage irradiation."

Fletcher *et al.*,[7] Jacox,[16] Lampe,[20] Lenz,[21] Moss,[24] and Nickson[27] also find no statistically valid evidence of better results in laryngeal cancer with supervoltage therapy.

Our own experience with laryngeal cancers includes some 175 patients, treated by orthovoltage roentgen therapy. The majority of these were intrinsic squamous cell carcinomas (Fig. 5, *A*, *B* and *C*). The five year determinate cure rates in this group are: Stage I (single cord, without fixation), 88 per cent; Stage II (both cords, or single cord with fixation), 79 per cent; and Stage III (one or both cords, with invasion or metastases), 33 per cent.

Some of the radiation failures were successfully treated by subsequent laryngectomy.

The five year cure rate for all intrinsic lesions was 46 per cent; for extrinsic tumors it was considerably less.

Tonsil: Sheline *et al.*[36] report a series of 56 patients treated for cancer of the tonsil; the five year survival rates after orthovoltage therapy were 20 per cent and after megavoltage therapy 20 per cent.

Tapley *et al.*[40] also report a series of tonsil carcinomas treated with both modalities; in 71 male patients the five year survival rates were 21 per cent in each group. They write, "There is no evidence that the form which the radiation therapy of the primary lesion takes (radium alone, radium and roentgen ray, orthovoltage, or supervoltage external therapy alone) has an important effect on the outcome."

Alveolus and Antrum: Paterson[29] reports 42 patients treated with 4 mev. roentgen rays. The two year cures were approximately 42 per cent, "not significantly different from earlier results using 250 to 500 kv. radiation."

B. ESOPHAGUS

Fletcher *et al.*,[7] Friedman,[34] and Philips[31] find no evidence of increased cure rates with supervoltage therapy. Fletcher writes, "Large series of cancers of the esophagus and lung treated with supervoltage have failed to show any appreciable improvement in results when compared with con-

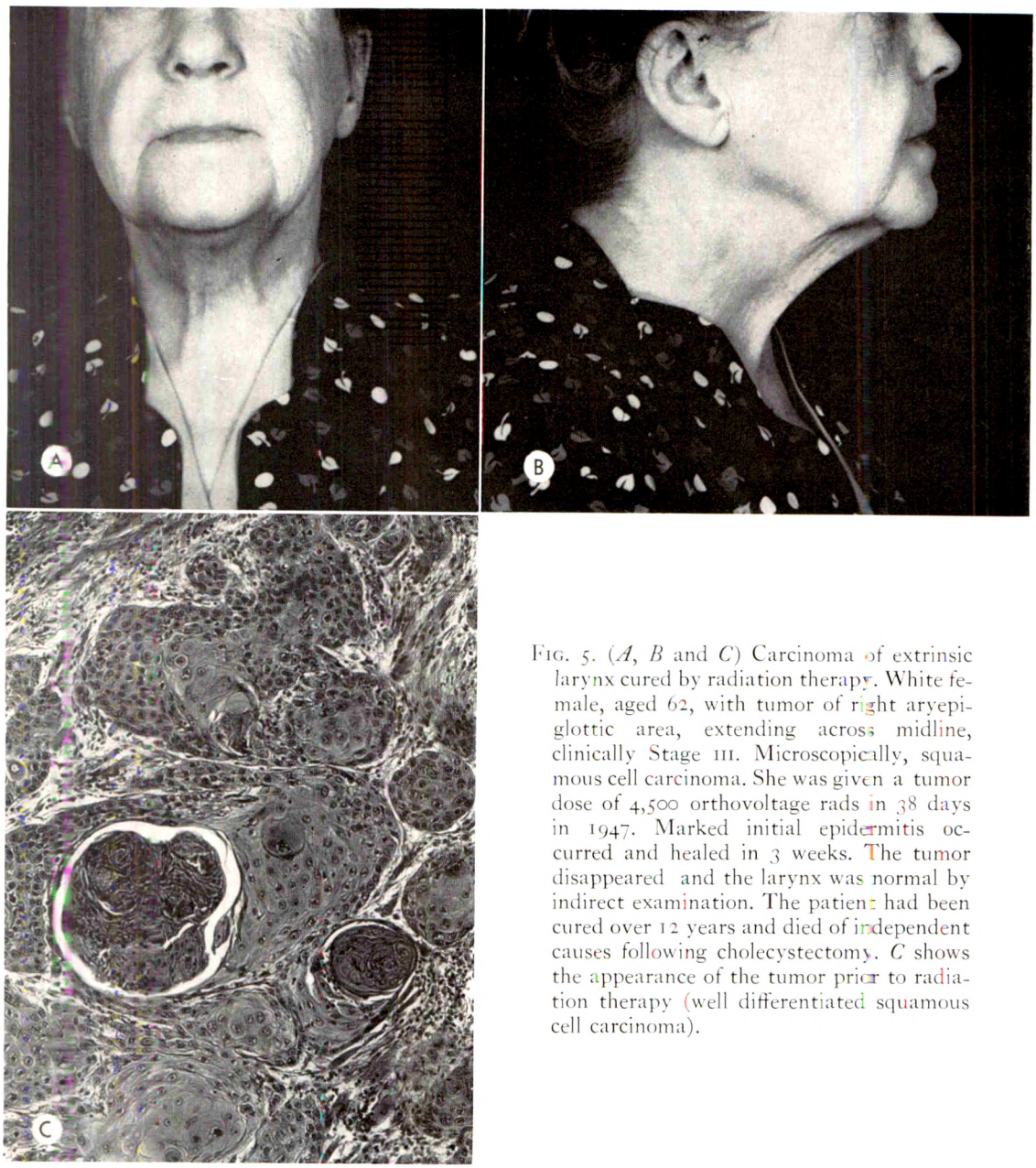


Fig. 5. (*A*, *B* and *C*) Carcinoma of extrinsic larynx cured by radiation therapy. White female, aged 62, with tumor of right aryepiglottic area, extending across midline, clinically Stage III. Microscopically, squamous cell carcinoma. She was given a tumor dose of 4,500 orthovoltage rads in 38 days in 1947. Marked initial epidermitis occurred and healed in 3 weeks. The tumor disappeared and the larynx was normal by indirect examination. The patient had been cured over 12 years and died of independent causes following cholecystectomy. *C* shows the appearance of the tumor prior to radiation therapy (well differentiated squamous cell carcinoma).

ventional therapy, provided that comparable clinical material has been evaluated."

Friedman[34] noted that the first 40 cases of esophageal cancer he treated with supervoltage rotation died within less than two years "which is poorer than several reported groups with 200 kv."

Our experience with esophageal cancer included some 200 patients, treated by orthovoltage roentgen therapy, and a few patients with rotational telecobalt therapy. There are no five year cures. The palliation rate was as good with fixed-field roentgen rays as with rotational cobalt therapy to date.

c. lung

Fletcher *et al.*[7] and Philips[31] report no increase in arrests and no significant increase in palliation with supervoltage ther-

apy. Jacox[16] writes ". . . with multimillion volt machines or cobalt beam therapy there has been no significant increase in (lung cancer) cures . . . Nothing can be gained by supervoltage therapy that cannot be obtained by careful planning and treatment application at deep therapy voltages." It is noted that pulmonary reaction and esophageal injury are more apt to occur with supervoltage therapy. Philips[31] reports that "Bronchogenic cancer, like cancer of the esophagus, has proved just as intractable to supervoltage as to medium voltage therapy . . ."

We have reported our experiences with primary bronchial cancer treated by orthovoltage roentgen therapy. Out of some 150 patients there are only 2 five year survivals to date. However, the temporary palliation rate in terms of relief of cough, pain and hemoptysis ranged from 60 to 75 per cent (Fig. 6, *A–D;* and 7, *A* and *B*). Average survival time following radiation therapy was about double that in the untreated group (*i.e.*, 7 versus 3.5 months). Our results with telecobalt therapy to date are not significantly different, the median survival being less than seven months.

D. UTERINE CERVIX

Hunt *et al.*[15] using orthovoltage therapy plus intracavitary radium, report 59 per cent five year absolute arrests in 246 cases. Murphy,[26] using megavoltage therapy plus radium in a series of 1,244 cases, reports 51 per cent five year arrests. If one considers the more localized cases, one finds the following five year arrest figures reported by these authors.

	Stage I (per cent)	Stage II (per cent)	Stage III (per cent)
Orthovoltage Therapy (Hunt *et al.*[15])	87	60	35
Megavoltage Therapy (Murphy[26])	75	55	36

These data show no increase in cure rate in cervical cancer with megavoltage therapy.

Stone[38] reported that his five year results in 35 patients treated with 200 kv. were superior to those in 35 comparable cases treated with 1,000 kv. roentgen rays.

We have treated several hundred patients with cervix cancer using a combination of radium and orthovoltage roentgen therapy. In recent years our five year survival rate in treated patients has ranged from 44 to 49 per cent. Except in unusually thick or obese patients, it is not evident that cobalt or megavoltage therapy *per se* will significantly improve these results (Fig. 8, *A* and *B;* 9; and 10, *A* and *B*).

E. OVARY

Cancer of the ovary is difficult to diagnose and to stage; therefore the following figures are reported not as definitive, but as suggestive data. Sisson and Garland, using postoperative orthovoltage wide-field roentgen-ray therapy had 23 per cent five year survivals in 115 cases; Murphy[26] using postoperative supervoltage roentgen rays had 19 per cent survivals in 95 cases—there is of course no significant difference in these figures.

F. BREAST

No writers claim superior results in breast cancer with megavoltage therapy. Indeed, Kaplan and Bagshaw[17] report returning to 140 kv. roentgen rays to irradiate the internal mammary chain; Meurk and Chu[25] report a study of cases treated with 250 kv. and 1,000 kvp., concluding that as far as the chest wall was concerned "the 250 kv. tangential technic delivered the least radiation to the lung." They did however, indicate a personal preference for megavoltage therapy in the supraclavicular area.

Bachman and Macken[1] noted a significant increase in pulmonary fibrosis and pleural reactions with supervoltage-treated breast tumors. They regarded the effusions as being radiogenic in 5 per cent of cases.

For cutaneous lymphatic permeation, orthovoltage would have obvious advantages compared with megavoltage (Fig. 11, *A–D*). However, for the high axillary region in unusually thick patients (especially

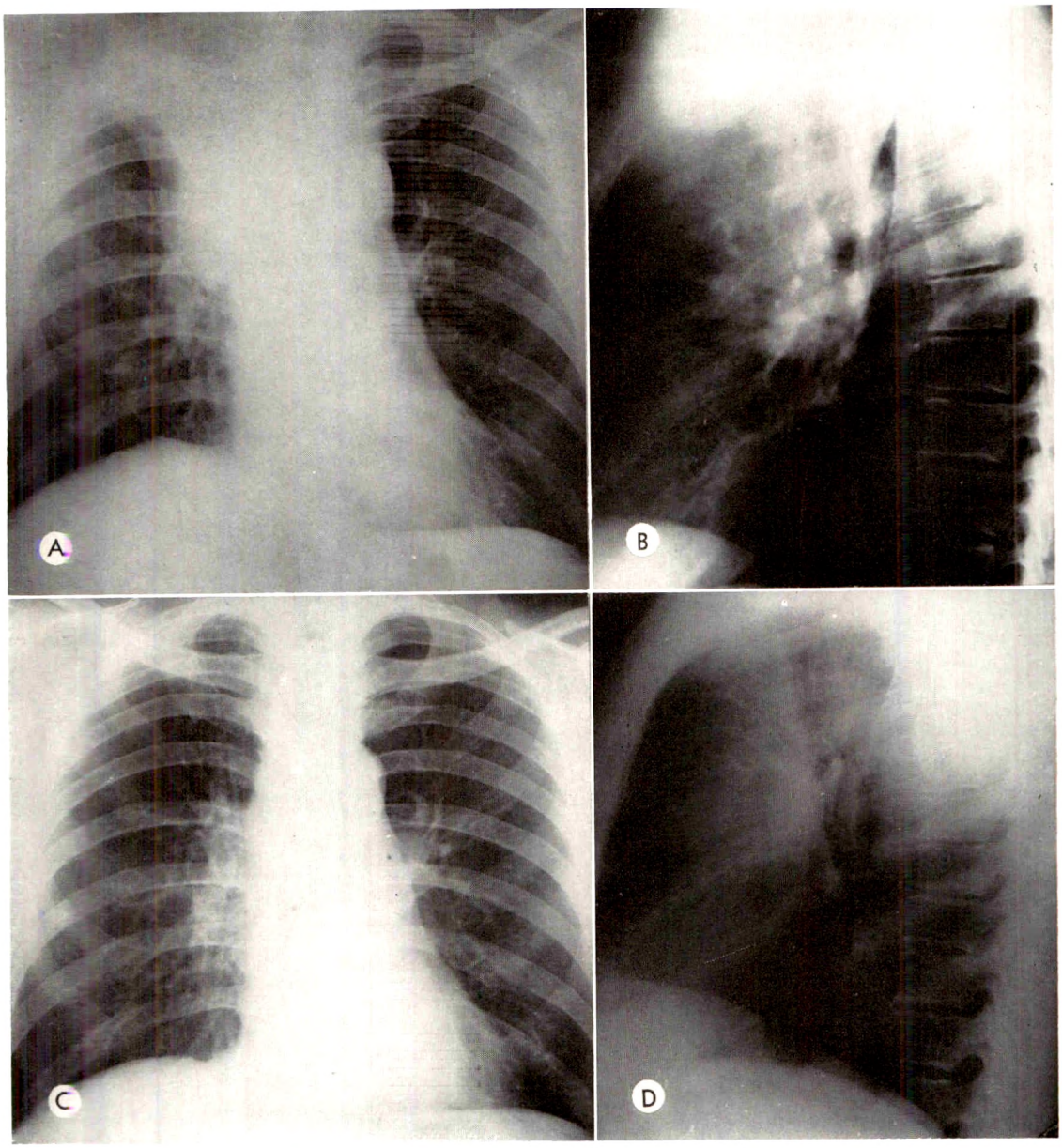


Fig. 6. Primary lung cancer, locally cured by radiation therapy. Male, aged 56, with cough, hemoptysis and weight loss. (*A* and *B*) Roentgenograms show atelectasis of right upper lobe. Bronshoscopy showed a tumor in the right upper lobe bronchus. The carina was fixed and the lesion was regarded as inoperable. Pathologic diagnosis, anaplastic carcinoma. (*C* and *D*) Three months after radiation therapy (3,500 orthovoltage rads tumor dose, in 4 weeks, to an oval area 14 cm. in diameter). The atelectasis has cleared up. The patient returned to work, gained weight and lived for slightly over one year, when he died of cerebral metastases.

in the absence of radical surgery), megavoltage should permit simpler and more effective irradiation.

G. BLADDER

Friedman[9] reports a 13 per cent five year arrest rate in patients treated with megavoltage beams (which he considers much inferior to the 56 per cent rate he previously had obtained with intracavitary radioactive sources).

Paterson[29] and Pointon[32] report results of

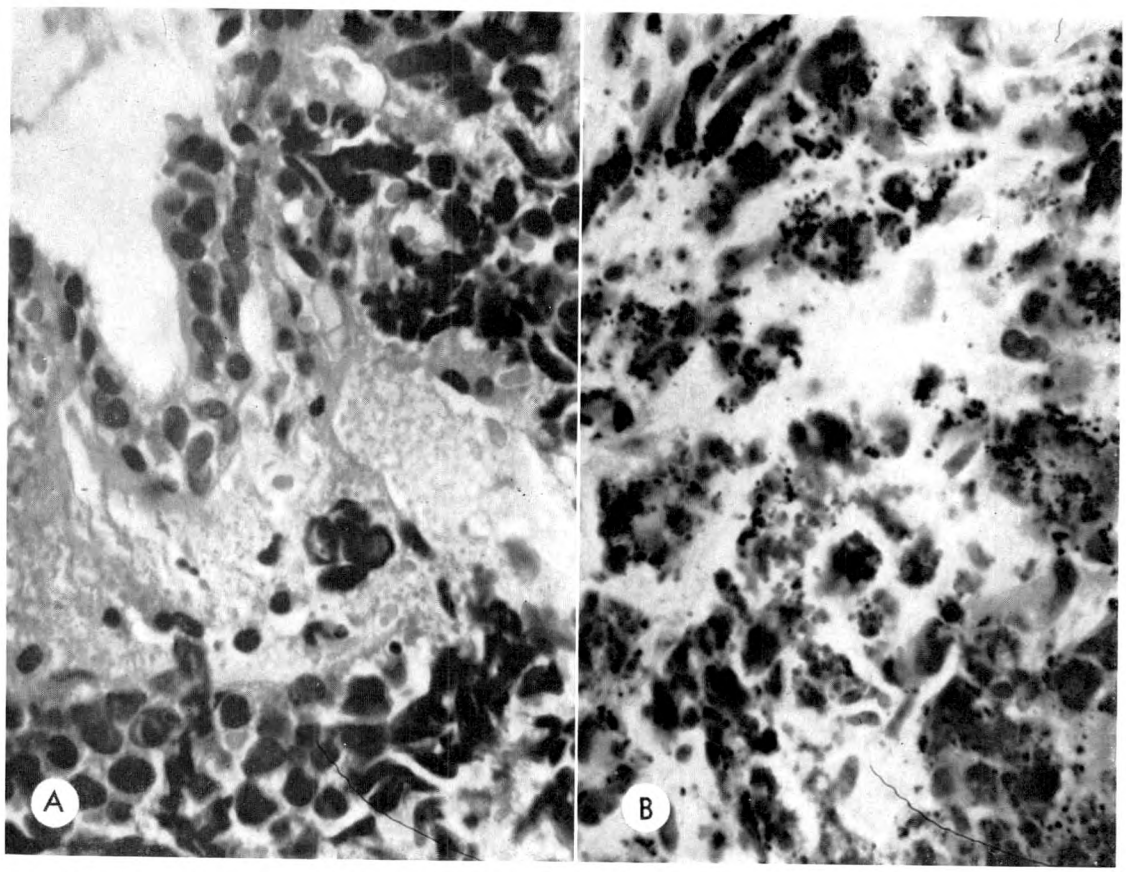


Fig. 7. Same patient as shown in Figure 6. (*A*) Tissue shows epidermoid carcinoma of the right upper lobe bronchus, anaplastic. (*B*) Tissue from same portion of bronchus at autopsy, a little over 12 months later. There is no microscopic evidence of viable tumor cells in the irradiated area. A minority of epidermoid carcinomas of the bronchus are locally controllable with tissue doses in this range. (Figures 6, *A-D* and 7, *A* and *B* courtesy of Garland and Sisson, *Radiology*.)

radical 4 mev. treatment of 87 patients with bladder cancer. The three year survival rate was 29 per cent—not significantly different from the 27 per cent rate obtained previously with premegavoltage roentgen rays in the 250–500 kv. range.

For localized cancer of the trigonal area, rotation therapy (using orthovoltage or megavoltage) should permit more effective irradiation. We have treated a small number of such patients with a 1,200 curie cobalt rotation unit, with an early tumor response not significantly different from that previously obtained with fixed-field orthovoltage therapy. Other investigators have commented on the relative low radiosensitivity of many bladder cancers—a fact which may explain the disappointing results of megavoltage therapy to date.

H. BRAIN

Peirce[30] reports a twenty year radiation therapy study of over 600 patients with primary neoplasms of the brain and brain stem. Palliation was reportedly good in about three-fourths of the gliomas treated with adequate dosage (about 5,500 orthovoltage rads in seven weeks time); medulloblastomas yielded 20 per cent ten year survivals. He writes: "Supervoltage therapy is not necessary and has no advantage other than some sparing of the radiation dose to the scalp."

Several radiotherapists have used mega-

voltage radiation, with or without rotation, for pituitary adenomas. Their published results are not any better than those obtained with orthovoltage. Using three fields and tumor doses of about 3,000 orthovoltage rads in three to four weeks time, we have treated some 45 cases of pituitary adenoma (mostly chromophobic) with excellent results.

These various data on the relative results actually obtained with orthovoltage and megavoltage radiation (Table II) confirm the observation of Kaplan,[18] published in 1958, that "there has not been any conclusive demonstration that supervolt-

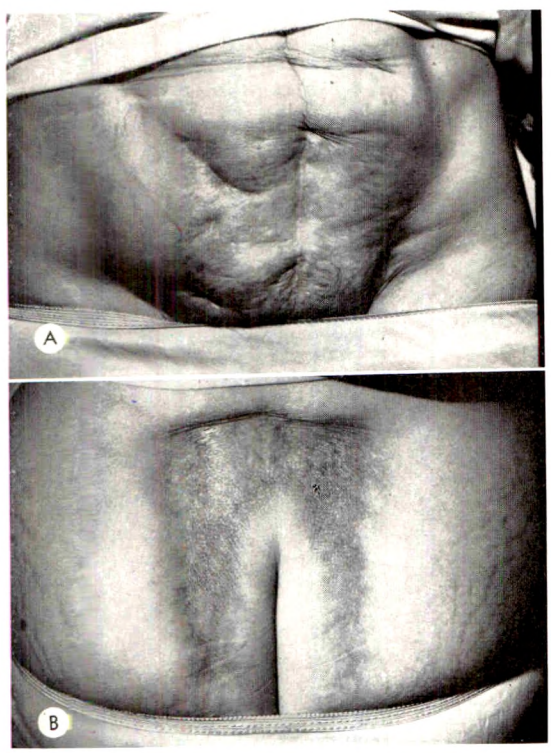


FIG. 8. (*A* and *B*) Example of skin and subcutaneous tissue changes 7 years after megavoltage radiation therapy. White female, aged 47 in 1952, was treated in that year for Stage II carcinoma of the cervix by 1 mev. roentgen-ray beam, to a dose of approximately 4,000 r in air, to each of 4 fields 8×15 cm. in 29 days and coincidental intracavitary radium therapy. These photographs were made 7 years later. The patient now has marked subcutaneous fibrosis over the pelvis, slight telangiectasis, and painful radiation osteitis of the sacrum and fifth lumbar vertebra.

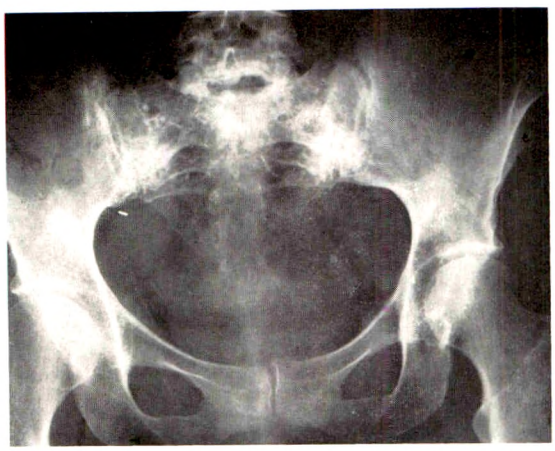


FIG. 9. Roentgenogram of the patient shown in Figure 8 made 7 years after the course of megavoltage radiation therapy shows patchy sclerosis of the sacrum and fifth lumbar vertebra, indicative of radiation osteitis. She had rather severe pain. No clinical or cytologic evidence of recurrent neoplasm was noted.



FIG. 10. (*A* and *B*) Example of skin changes 7 years after orthovoltage radiation therapy. White female, aged 49 in 1952, was treated in that year for Stage III carcinoma of cervix by orthovoltage therapy (200 kv., half value layer 2 mm. copper) to a dose of 2,500 r in air to each of 7 fields 10×15 cm. in 46 days. These photographs were made 7 years later. The patient has telangiectasis, but no significant degree of subcutaneous fibrosis, and there is no evidence of radiation osteitis. These skin changes are usually less disabling than the severe subcutaneous fibrotic changes sometimes seen after megavoltage therapy.

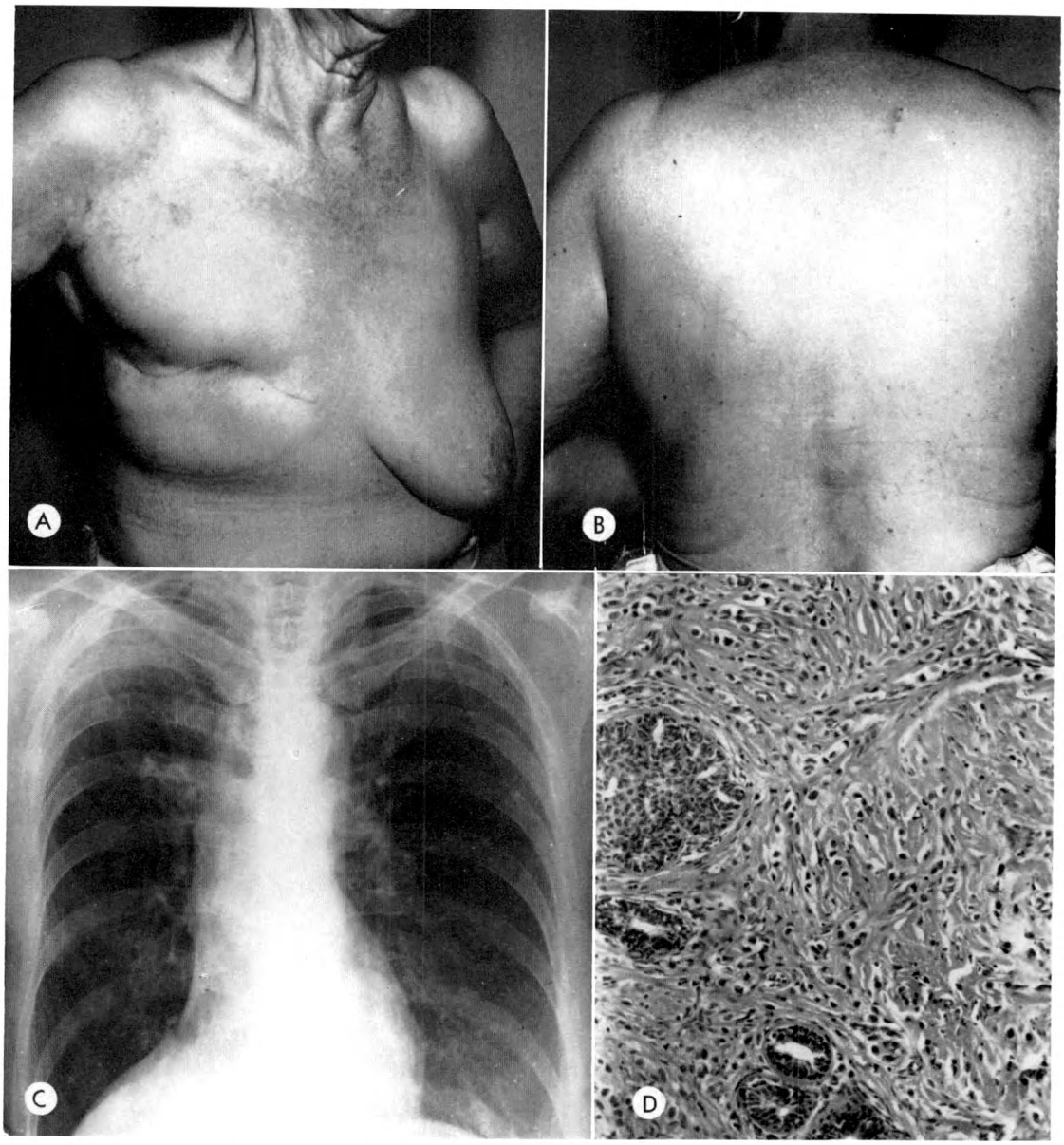


Fig. 11. Mammary carcinoma, locally controlled by simple mastectomy and orthovoltage radiation therapy. Mrs. N. K., aged 57, with Stage 1 carcinoma of right breast treated by simple mastectomy and postoperative radical radiation therapy. (*A* and *B*) Photographs made 5 years after treatment show minimal residual telangiectasis. (*C*) Chest roentgenogram 5 years after treatment shows no pulmonary fibrosis. (*D*) Histologic appearance of primary tumor (adenocarcinoma) at the time of operation. (Courtesy of *Radiology*.)

age therapy yields a significantly improved cure rate for any particular variety of cancer," and of Martin[23] that "supervoltage machines neither increase the cure rate nor reduce the number of secondary internal sequelae. . . ." Quastler[33] and many others have stressed that the biology of the particular cancer under treatment is the more important factor.

COMPLICATIONS

The complications of radiation therapy may be listed as early and late, local and general. They include erythema, telangi-

TABLE II

SUMMARY OF COMPARABLE CLINICAL RESULTS WITH ORTHOVOLTAGE AND MEGAVOLTAGE THERAPY

Author	Tumor Site	Orthovoltage Therapy (200–400 kv.) (per cent*)	Megavoltage Therapy (1,000–6,000 kv.) (per cent*)
Cantril[3]	Larynx	55	41
Shelline *et al.*[30]	Tonsil	20	20
Friedman[31]	Esophagus	0	0
Philips[31]	Lung	0	0
Hunt *et al.*[15]	Cervix	59	
Murphy[26]	Cervix		51
Poinsett[32]	Bladder	27	29

* All data represent five year survival rates except those for the bladder, for which three year survival rates are shown.

ectasis, atrophy, fibrosis, necrosis, pain, nausea, vomiting and even late neoplasia. Fibrosis of deep structures may lead to pericardial, pulmonary, intestinal, neurologic, osseous and other disorders. Necrosis may lead to perforations of hollow viscera, destruction of cartilage or bone, and secondary infections. As with radical curative surgery, a *small* incidence of such complications must be accepted as unavoidable, in the light of the good done the major number. For example, almost 50 per cent of women with uterine cervical cancer (all stages combined) are now curable by effective radiation therapy; the incidence of severe radiation proctitis, ileal fibrosis or femoral neck osteitis is about 4 per cent, or 2 out of every 50 women cured. This compares more than favorably with the complication of ureteral necrosis or obstruction following radical hysterectomy for this disease, reported by its leading proponent as 14 per cent.

Complications must and can be minimized by avoidance of excessive total dosage, and of unduly rapid or intensive dosage. With judicious protraction of treatment, meticulous daily administration and correct associated care, they can be kept to a minimum, whether orthovoltage or megavoltage irradiation is used. However, without care and experience, they are more apt to occur with supervoltage therapy because of the deceptively mild early skin reactions.

Late reactions following supervoltage radiation therapy have been recently reviewed by Leucutia.[22] He writes: "There is accumulating evidence that by using supervoltage radiation therapy . . . indolent fibrosis may be developing in deep seated structures where elastic or areolar connective tissue forms a supporting stroma, and that this indolent fibrosis may be a causative factor . . . accounting for the late changes observed in the parenchyma of an organ or in the basic elements of a system . . . In using supervoltage radiation therapy over the chest, the chances of similar reactive changes are greatly increased." He refers to reports of radiation pneumonitis with fatal outcome, gastrointestinal tract injuries, and urinary tract reactions. He notes the occurrence of radiation myelitis after supervoltage, and the fact that the incidence of radionecrosis of bone and cartilage (following irradiation of head and neck lesions) is similar to that from orthovoltage roentgen therapy.

CHOICE OF MODALITY

Effective radiation therapy requires the deliverance of an adequate but tolerable dose to the diseased area of interest. This may be accomplished by one or a combination of many different modalities. With 200 kv. (orthovoltage) beams, it is possible to deliver such doses to the deeper tissues of most patients without permanent and serious damage to the normal structures near the tumor and without irreparable damage to the overlying skin. Therefore, the radiotolerance of the skin is *not* the limiting factor in deep therapy; it is rather the anatomic extent of the tumor and the relative radiosensitivity of the tumor cells.

For persons who are unusually thick (over 30 cm.) or whose skin overlying the tumor has had serious prior injury, megavoltage beams do have a usefulness by virtue of their better penetration and decreased skin effect, providing nonopposing

fields are used. For rare lesions such as sharply localized posterior retinal tumors, they also have a definite physical advantage. However, in most cases, literal "pin-pointing" of the beam is neither useful nor sensible. "Pin-pointing" of radiation beams has been utilized for four decades, daily in the case of superficial lesions, seldom for deep-seated lesions because their precise anatomic extent is difficult to ascertain, and literal pin-pointing might result in not irradiating large portions of the tumor.

The importance of *visible* biologic reactions is stressed by Glicksman, Chu, Bane and Nickson[13] after a study of patients treated by protracted irradiation: "Experienced radiotherapists will recall patients whose reaction to irradiation systemically or locally was so vigorous as to necessitate termination of treatment after only two-thirds or three-fourths of the usual time-dosage relationship accepted by most patients. In some, the response of the tumor appeared to correlate better with the severity of the biological response than with the physically measured amount of energy delivered to the patient. . . .

"It would appear from the foregoing that a biological triage of responsiveness to ionizing radiation, at least as far as the skin is concerned, does in fact exist. The correlation of these observed classes with other kinds of biological response, *i.e.*, degree of late fibrosis and, perhaps most important, tumor response, must await further studies of these and similarly identified patients. It seems probable that the vigor of reaction of tumor cells to irradiation will be found in the end to correlate more with biological factors than with physical factors."

Orthovoltage beams are regarded as indicated for many if not most patients with neoplastic disease suitable for radiation therapy because with them there is:

(a) *Increased Accuracy of Dose Administration.* Flexible orthovoltage units permit the radiologist to adjust the beam readily to the patient; cumbersome megavoltage units often require adjusting the patient to the beam. Orthovoltage therapy fields can be precisely tailored to the individual case with simple diaphragms or lead sheets; megavoltage units call for cumbersome collimators or lead blocks.

(b) *More Precise Definition of Beam Margin.* Orthovoltage units, when used with cones and skin shields, permit sharp definition of beam edges. Some megavoltage units (notably cobalt and cesium teletherapy units) have ill-defined beam edges owing to large penumbra. Indeed, with small treatment fields, the latter can render the megavoltage device physically less efficient than the orthovoltage unit. There is better protection of normal beam-adjacent structures with many orthovoltage beams. This does not apply to megavoltage roentgen-ray devices utilizing small focal spot tubes.

(c) *Better Protection of Deep Structures.* Skin erythema is a useful clue to tissue tolerance. With warning skin reactions, deep tissues are better protected. Serious late subcutaneous fibrosis, neurologic injury, pulmonary fibrosis and gastrointestinal injury have been reported with megavoltage despite an intact overlying skin. For most persons, skin tolerance is *not* the limiting factor in radiation therapy. With megavoltage, the high exit dose in thin parts such as the neck, may result in excessive dosage.

(d) *Comparable Tolerance.* With orthovoltage radiation, absorption in cancellous bone and bone marrow is closely similar to that from equal doses of megavoltage radiation; however, scatter and presumably absorption in compact bone is greater than that with megavoltage. This last phenomenon may be an advantage and not a disadvantage—for example in treating lesions such as diffuse osseous metastases. The incidence of postradiation osteitis and bone necrosis following radical radiation therapy is apparently about equal with the two modalities, when biologically equal doses are employed.

(e) *Decreased Incidence of Late Subcutaneous Injury.* Orthovoltage beams usually produce maximum ionization in the

skin; after radical therapy there may be late telangiectasis and atrophy. This can be followed carefully, and treated medically or surgically when indicated. Megavoltage beams produce maximum ionization in the subcutaneous tissues (at about 0.5 cm. depth with telecobalt and about 1.5 cm. depth with 4 mev. linear accelerator beams); after radical megavoltage therapy there may be late fibrosis and atrophy of the deep subcutaneous tissues. These are lesions difficult to assess and to treat. If neoplastic change eventuates (*e.g.*, fibrosarcoma), the lesion may be less amenable to cure than an observable skin injury resulting from heavy orthovoltage therapy.

DISCUSSION

In 1932, the roentgen came into general use as a unit of roentgen-ray measurement. Doctors were often impressed to learn that their patient had received a large dose, *e.g.*, 8,000 r. A little inquiry might have elicited the fact that this referred to the air dose of all exposed fields added together—not the actual tumor dose. But the large numbers were impressive to the uninitiated.

In 1933, after trial of a *10 gm. radium bomb* at the Curie Institute, del Regato and Regaud[6] concluded that "it showed no important superiority over lower potential roentgen therapy which was more elastic and less dangerous to all concerned."

Almost thirty years later the same can be said, in general, for cesium units, cobalt units, linear accelerators and multi-million volt roentgen-ray therapy units. But the large numbers—6 million volts, 10 million volts, 90 million volts still impress our colleagues, even though the tumor effect is not increased and indeed the biologic efficiency of the megavolt rad is actually decreased.

In 1938, after several years use of million volt radiations, Stone[39] stated "It is my belief that, with a proper use of 200 kv. radiations, as much effect can be produced in the interior of all but the thickest patients, as their tissues will stand. Progress is to be made not by increasing voltage but by changing such factors as protraction. . . ."

For all accessible, and many nonaccessible, localized radiosensitive tumors, a cancericidal dose can be given with orthovoltage rays. The ease of administration of such dose is enhanced in sites such as cervix, tongue and antrum by associated intracavitary or interstitial gamma-ray therapy. The two agents, orthovoltage roentgen rays and localized gamma rays, constitute the modality of choice in most clinical situations. Nickson,[27] discussing the remarks of Stone and Quastler at the Highland Park Radiation Conference, summarized matters by stating that perhaps the orthovoltage unit "used with care and thought, and used to its limit, may be a lot better than we really think it is." And Constance Wood observed at the 1959 International Radiology Congress that the over-all survival rates with the 8 mev. linear accelerator are not superior to those obtained in a comparable series of cases treated with 250 kv. therapy.

CONCLUSIONS

1. Irradiation of cancers suitable for radiation therapy can be performed effectively with many different modalities—ranging from low voltage roentgen-ray machines to ultra-high voltage electron beam devices, depending on the size, depth, type and location of the tumor and the status of the surrounding tissues. For most deep-seated cancers, patient safety tends to be greater with orthovoltage therapy.

2. The biologic type of the tumor present and the host's defense mechanism are more important than the voltage employed. This has been expressed in the 60–30–10 "law"—which states that the factors influencing the radiologic cure of cancer reside about 60 per cent in the nature and extent of the tumor, about 30 per cent in the skill and experience of the radiologist, and about 10 per cent in the modality employed.

3. There is but little validity to the claim that supervoltage therapy permits an effec-

tive dose with less risk of complications and less general discomfort to the patient (when doses biologically equal to those delivered with orthovoltage rays are used). There may be less initial local cutaneous discomfort with supervoltage therapy, but this tends to be offset by greater ultimate subcutaneous injury.

4. Supervoltage or megavoltage devices may be described as "heavy on promise but light on performance," yet not undeserving of continued scientific investigation under research and preferably controlled conditions—wherein long-term results with human cancer would receive scientific study and deliberate publication.

5. Clinical indications for the use of several types of modality are considered in this paper, and it is shown that, for most neoplastic problems, orthovoltage (200 kv.) roentgen-ray machines plus radium in suitable sources still constitute very effective means of modern radiation therapy.

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ANGIOGRAPHIC HYPERVASCULARITY AND SURVIVAL IN GLIOBLASTOMA MULTIFORME*

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ABUNDANT neoplastic vascularity often is visualized on the cerebral angiogram of a glioblastoma multiforme. In addition to the obvious diagnostic implications in the roentgenographic demonstration of tumor vessels, a richly vascularized glioblastoma provides a clue to a histologic subdivision within the glioblastoma group itself.

In a study of 133 glioblastomas, Busch and Christensen[1] included 74 cases with cerebral angiograms. All but 1 of the 22 tumors with "arteriovenous anastomoses" seen on angiograms were also found to have intense vasculo-proliferative histologic changes (their so-called "angionecrotic" classification). Other investigators have also found parallelism in comparing roentgen and histo-angioarchitecture in this tumor. Cuccia[2] recently considered these features in 59 cases and found that all of the tumors with abundant coarse new vessel formation seen on the cerebral angiogram were likewise highly vascularized on histologic examination, while of the cases with no neoplastic vascularity seen angiographically, 73 per cent showed sparse neovascularity histologically.

A definite parallelism between histologic malignancy and the degree of endothelial hyperplasia in the astrocytoma-glioblastoma group of brain tumors is well recognized and occasionally the hyperplastic endothelial cells in some glioblastomas may themselves assume neoplastic properties and even form sarcomatous tissue.[3] The pathogenetic mechanisms of the peculiar and often bizarre vascular formations observed in glioblastoma are controversial and beyond the scope of this paper.

Since vascular proliferation is intimately related to malignancy in glioblastoma and since there seems to be a correlation between histologic and angiographic studies in vascularization, it follows that the cerebral angiogram *alone* might well be utilized in the analysis of yet another aspect of relative malignancy in this tumor, namely, survival. The purpose of this study is simply to compare angiographic vascularity with longevity in a series of proved cases of glioblastoma.

MATERIAL

Eighty-two cases of histologically proved glioblastoma multiforme with positive cerebral angiograms were reviewed. For simplification, they were separated according to the angiographic findings into two large groups: (1) those demonstrating rich neovascularity in the form of numerous large caliber tumor vessels, "sinusoids," or arteriovenous connections (hypervascular); and (2) those with only relatively few or completely absent tumor vessels (avascular). No attempt was made at further angiographic subdivision, although it is realized that various classifications have been offered, largely for diagnostic purposes.[4,5] The post-operative survival times of each group were recorded and compared.

Twelve patients survived only five post-operative days or less and were rejected as operative deaths. Ten angiograms demonstrated nonfilling, spasm or marked compression of the arterial distribution to the vicinity of the neoplasm and were likewise discarded, since the status of the vascularity within the tumor could hardly be established. Nine cases still living with a post-operative survival time of less than fifteen months were excluded.

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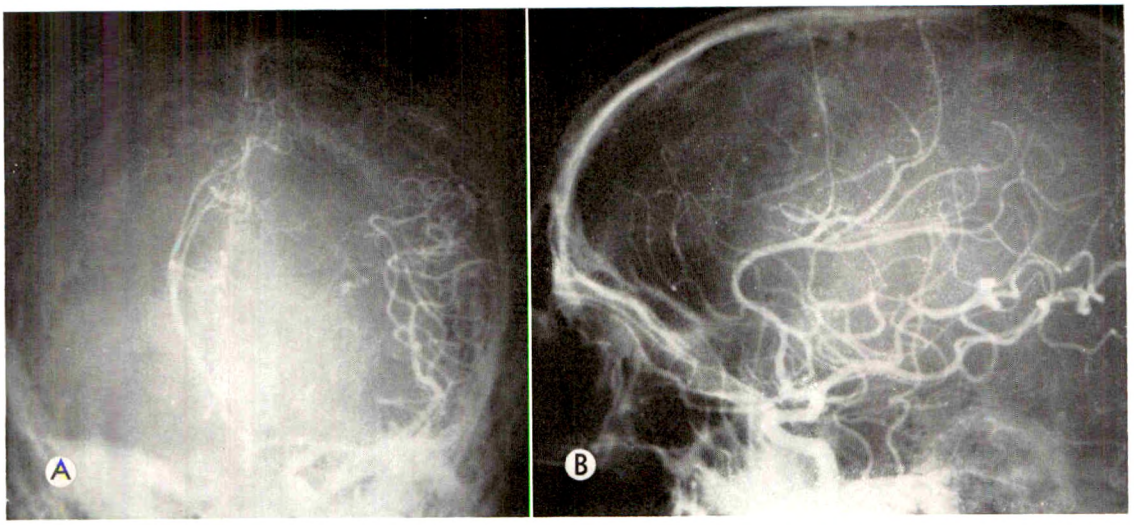


Fig. 1. (*A* and *B*) Avascular glioblastoma in the left frontal lobe. Survival time, thirteen months.

RESULTS

Of the remaining 51 cases with angiograms suitable for this study, 37 cases (72.6 per cent) were found to have scanty or absent vascularity, while 14 cases (27.4 per cent) demonstrated abundant coarse new vessel formation on the angiogram. An example of each angiographic group is presented briefly for illustration.

Case I. P. W., 25358, a forty-three year old Negro male, was admitted with symptoms of three weeks' duration. A left carotid arteriogram revealed a large mass in the left frontal lobe with no appreciable tumor vascularization (Fig. 1, *A* and *B*). A craniotomy the next day was followed by subtotal resection of a large left frontal lobe glioblastoma. The patient expired thirteen months later.

Case II. D. S., E-73716, a forty-seven year old Negro female, developed symptoms five months prior to admission. A left carotid arteriogram demonstrated an extensively vascularized tumor in the left frontal lobe (Fig. 2, *A* and *B*). The same day a glioblastoma was partially resected from the left frontal lobe. The survival time was four post-operative months.

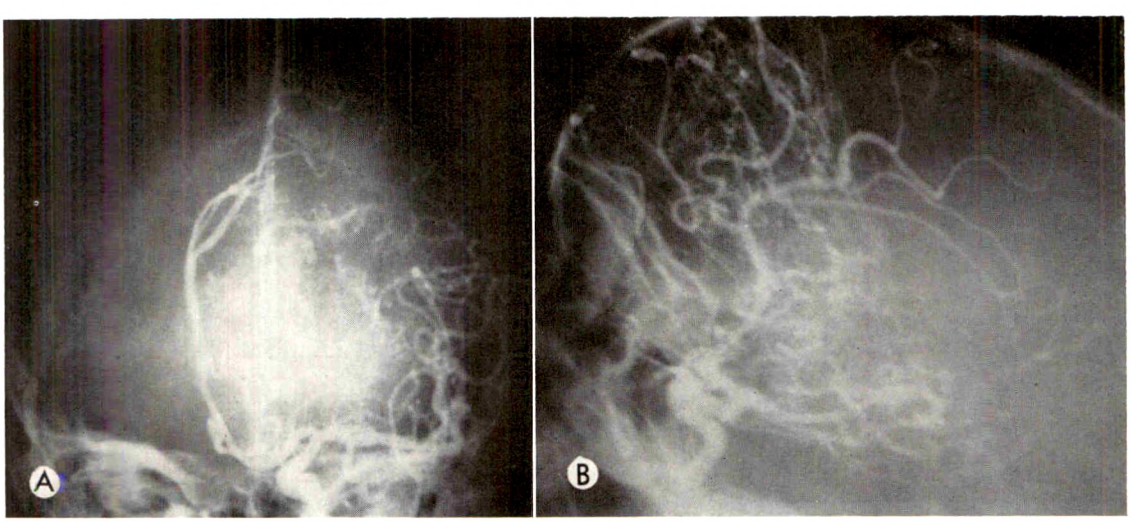


Fig. 2. (*A* and *B*) Hypervascular glioblastoma in the left frontal lobe. Survival time, four months.

Case I represents the angiographically classified avascular glioblastoma, while Case II is a typical example of the hypervascular tumor. Figure 3 charts the percentage survival of each group for the postoperative months survived. These percentages are also compared in Table I. A difference in longevity is apparent with no survivor in the hypervascular group at nine months after surgery. Fourteen per cent of the avascular cases survived one year and 1 patient is still living forty-three months after surgery.

DISCUSSION

While most of the previous angiographic studies on glioblastoma have concentrated on the diagnostic features of the angioarchitecture, there are few data on an angiographic-survival correlation. The 60 "angionecrotic" cases in Busch and Christensen's[1] series (33 with angiograms) had the poorest comparative prognosis, but the authors did not directly relate the survival data to the angiographic material.

Undoubtedly, some of the avascular cases in this series would have demonstrated tumor vessels at serial angiography and, indeed, delayed exposures have revealed neovascularity in a few of the cases included here. For the purpose of uniformity, the few tumors showing significant new vessel formation only in the "capillary" phase of cerebral circulation are included in the avascular group. The extent of the operative procedures were comparable in the two groups.

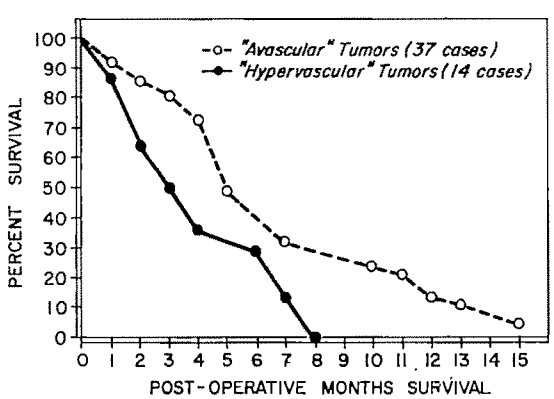


Fig. 3. Angiographically classified tumor vascularity and survival in 51 glioblastomas.

Table I

ANGIOGRAPHIC TUMOR VASCULARITY AND SURVIVAL IN 51 GLIOBLASTOMAS

Post-operative Survival (mo.)	Hypervascular Tumors (14 cases)		Avascular Tumors (37 cases)	
	Per Cent Survival	No. of Cases	Per Cent Survival	No. of Cases
3	50	7	81	30
6	29	4	49	18
9		0	24	9
12		0	14	5
15		0	5	2

The vascularity-survival data as presented here suggest a malignancy differential in glioblastoma. The results are not intended to accurately represent absolute survival times in cases of this tumor, but only to provide comparative information obtained from two angiographic groupings.

Statistical analysis was not attempted in this small series and any prognostic value of this indication of shorter survival when there is gross angiographic vascularity is obviously limited in the individual patient. The results only emphasize the significance of the angiographic findings when they are considered with the clinical and histologic features of glioblastoma in the study of tumor biology.

SUMMARY

A comparison of cerebral angiograms with survival data in 51 cases of histologically proved glioblastoma multiforme has demonstrated shorter longevity in the group with gross hypervascularity as seen on the angiogram. This supports previous studies on the correlation of histologic malignancy and the intensity of vascular formation in this tumor as well as those stressing the parallelism between its histo-angioarchitecture and roentgen angioarchitecture.

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THE ROENTGEN THERAPY OF PONTINE GLIOMAS*

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PONTINE gliomas constitute perhaps 10 to 15 per cent of all brain tumors in childhood. Unfortunately, the vital location of these lesions obviates the possibility of surgical removal. Bailey, Buchanan and Bucy[2] wrote, "until some effective treatment other than surgical is devised, gliomas of the brainstem will be hopeless problems for treatment." Ingraham and Matson,[9] in reporting 30 cases of pontine glioma, felt that some palliation was obtained with radiation therapy. Bray, Carter, and Taveras[5] noted improvement following irradiation in the majority of cases. Bouchard[4] stated that most brainstem lesions are, "radiosensitive to varying degrees." Frequently, the results of irradiation of brain tumors have been analyzed by histologic groups, but not by location, making the value of roentgen therapy for these lesions difficult to determine. This report is an analysis of 42 cases of pontine gliomas seen from 1936 through 1959, with emphasis on the methods and results of roentgen therapy.

CLINICAL FEATURES

Age. The ages in our series ranged from three to fifty-three years. Twenty-nine patients (70 per cent) were in the three through ten age group. Seven patients were over twenty-one years of age. That no patient was less than three years old supports the reported rarity of the lesion before this age.

Race and Sex. There were 24 white patients and 18 Negro patients. Males outnumbered females 23 to 19. No race or sex predominance has been found in the reported cases.

Symptoms and Signs. Most of the cranial nerve nuclei, as well as ascending and descending tracts connecting the cerebrum with the cerebellum and spinal cord, are located in the brainstem. The wide variety of neurologic signs and symptoms which can result from a lesion here might readily be anticipated.

TABLE I

FREQUENCY OF SYMPTOMS IN 42 CASES OF PONTINE GLIOMA

Symptom	No. of Patients
Gait disturbance	28
Dysphagia and dysarthria	20
Diplopia	18
Headache	17
Hemiparesis	16
Nausea and vomiting	16
Facial weakness	9
Dizziness and vertigo	6
Tinnitus and hearing loss	3
Head tilt	2

In contrast to tumors of the cerebellum and fourth ventricle, brainstem gliomas usually show no evidence of increased intracranial pressure until late, if ever.

Headache was the most common *initial* symptom (10 patients), followed by diplopia, abnormal gait and hemiparesis (7 patients each). Facial weakness, nausea and vomiting, dysphagia, dysarthria, and mental changes were less frequently listed as first symptoms.

Gait disturbance was present at some time in well over half the cases. Dysarthria and dysphagia, headache, hemiparesis and diplopia were other frequently noted symptoms (Table 1).

Duration of Symptoms. The duration from onset of symptoms until time of diagnosis ranged from two weeks to three years, 33 cases having had symptoms less than

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Table II

FREQUENCY OF CRANIAL NERVE INVOLVEMENT IN 42 CASES OF PONTINE GLIOMA

Cranial Nerve	No. of Patients
VII	28
VI	24
IX and X	21
V	9
XII	6
XI	3
VIII	3

six months, the remainder from six months to three years.

Neurologic Findings. At the time of diagnosis, cranial nerve involvement was present in all cases with seventh nerve palsy being most common (Table II).

Thirty-six patients had evidence of pyramidal tract involvement such as hemiparesis and Babinski's sign. Papilledema was present at the time of diagnosis in 9 patients. Sensory changes were quite rare in contrast to the multiplicity of motor changes. This observation supports the findings of Bray *et al.*[5]

ROENTGEN FINDINGS

The plain skull roentgenograms were interpreted as abnormal in 13 cases. Separation of sutures was present in 10 cases and increased convolutional markings in 4.

Ventriculography was considered diagnostic of pontine glioma in 18 of 23 cases in which it was performed. Characteristic posterior and upward displacement of the aqueduct and fourth ventricle was described by Lysholm[10] and later by Gardner and Shannon[8] (Fig. 1). In addition, some degree of ventricular dilatation was present in 10 cases.

DIAGNOSIS

The diagnosis of pontine glioma is not, in the majority of cases, based on histologic evidence. Because of the vital structures intimately related to these tumors, there is a high morbidity associated with biopsy. Ingraham and Matson[9] reported that of 21 patients who were explored, a biopsy was possible in only 5.



Fig. 1. Ventriculogram of a five year old Negro male shows characteristic posterior and upward displacement of the aqueduct and the fourth ventricle (verified by operative exploration).

Many patients seen during the first decade of this study did not have ventriculography. This procedure has been a standard part of the diagnostic workup since the late 1940's. Fourteen patients had either no air study or one which was considered nondiagnostic. Each of these patients had sufficiently characteristic clinical findings to justify their inclusion, however (Table III).

Pathologic findings at autopsy revealed 2 cases of glioblastoma multiforme, 2 spongioblastoma and one unclassified glioma. Biopsy was performed in 2 of 8 cases brought to surgery and revealed one oligodendroglioma and one glioblastoma multiforme.

Table III

MEANS BY WHICH DIAGNOSIS WAS ESTABLISHED IN 42 CASES OF PONTINE GLIOMA

	No. of Patients
Ventriculography	18 (3 confirmed at operation)
Operation	5
Autopsy	5
Clinical findings only	14

Table IV

SURVIVAL TIMES OF 30 PATIENTS RECEIVING ROENTGEN THERAPY FOR PONTINE GLIOMA

Tumor Dose	Patients		0–3 mo.	3–6 mo.	6 mo.–1 yr.	1–2 yr.	2–3 yr.	3–5 yr.	5 yr.-more
3,000–4,000 r	12	dead	1	3	2				
		living	1		1	2			2
2,000–3,000 r	12	dead	2	1	3	1	1		
		living	2						2
less than 2,000 r	6	dead	3	1	2				
		living							

ROENTGEN THERAPY

Thirty of the 42 cases received at least one course of radiation therapy. All of these were treated with orthovoltage roentgen rays (200–240 kv. peak), with quality varying from 1.1 mm. Cu half value layer to 3.3 mm. Cu half value layer.

In general, three ports were used: two lateral opposing and a single posterior (occipital) port. Fields 6×8 cm. rectangular or 7 cm. diameter circular were commonly employed.

The estimated tumor dose ranged from 1,000 r in two weeks to 4,000 r in four weeks. Most patients treated prior to 1950 received 2,500 r or less in two to three weeks. During the past decade a 3,000–4,000 r tumor dose in three to four weeks has been more commonly administered. The survival times of the 30 treated patients, who were divided into three groups according to the estimated tumor dose, are shown in Table IV.

Although the majority of patients died during the first year following treatment, 4 of 8 living beyond one year have survived five years or more (60, 62, 75 and 117 months; all living and well at the time of last examination). Review of these 4 cases reveals no obvious discrepancies from the typical findings in pontine gliomas. Two diagnoses were confirmed at operation (grossly, no biopsies taken), while the other 2 were established by ventriculography. The patient living and well 62 months after treatment had papilledema and separated sutures at the time of diagnosis, but had a characteristic air study (along with ventricular dilatation) as well as typical clinical features. The nearly normal lives which these 4 patients have enjoyed following therapy is worth emphasizing. The 3 children in the group were reported to be doing well in school, and the forty-one year old patient was leading a productive life when last seen.

The wide range of survival times among similarly treated patients raises the question of the influence of histologic types on prognosis. Ten of Buckley's[6] 25 cases of histologically verified tumors were classified as glioblastoma multiforme and had an average duration from onset of symptoms to death of only four months. Fourteen gliomas were slower growing and classified as protoplasmic or fibrillary astrocytoma or as spongioblastoma unipolare with an average survival of two years. Of the 7 cases with pathologic verification in our series, both the glioblastoma multiforme and the spongioblastoma groups lived less than two months after diagnosis. The single case of oligodendroglioma was living with no evidence of recurrence twenty-six months after receiving 3,500 r tumor dose in a five week treatment period.

TABLE V

CLINICAL RESPONSE OF 30 CASES OF PONTINE GLIOMA AFTER ROENTGEN THERAPY

Improvement following Therapy	No. of Patients
Considerable	12
Moderate	8
Slight or none	10

Any increase in survival time would mean little if not accompanied by remission of symptoms. Many patients responded to a marked degree with an essentially symptom-free interval after therapy (Table V). The degree of response relative to dosage is shown in Table VI.

Reporting definite improvement in 24 of 37 irradiated cases, Bray *et al.*[5] concluded that, "the repeated experience of having induced a clear-cut remission of neurologic symptoms and signs for a short period of time deserves emphasis." Ingraham and Matson[9] likewise felt that radiation therapy was of value in producing decided, though temporary, remissions.

Of 12 patients who received no roentgen therapy, 3 were lost to follow-up and the remaining 9 were dead within two months after diagnosis. These cases cannot serve as a control series, however, as most were not treated because they were considered terminal when first diagnosed.

DISCUSSION

The above data suggest that a tumor dose of less than 3,000 r, and certainly one less than 2,000 r, is below the optimal range. It has been evident from reports in recent years that an upper limit to the desirable dose range also exists. Boden[3] reported 7 patients with various head lesions who developed brainstem damage some months after radiation therapy which included the brainstem in the treatment volume. He felt a reasonable tolerance dose to the brainstem to be 4,500 r in seventeen days (or 5,000 r in thirty days) for a small volume. For a large volume the dose would be 3,500 r in seventeen days (or 4,000 r in thirty days).

TABLE VI

CLINICAL RESPONSE OF 30 CASES OF PONTINE GLIOMA AS RELATED TO THE TUMOR DOSE

Dose	Improvement following Therapy		
	Considerable	Moderate	Slight or none
3,000–4,000 r	6	3	3
2,000–3,000 r	5	3	4
less than 2,000 r	1	2	3

Arnold, Bailey and Harvey[1] reported 2 patients irradiated for brainstem gliomas with tumor doses of 4,500 r in thirty days (400 kv. radiation) in whom radionecrosis of the brainstem appeared after an interval of one year or more. They felt that 3,000 r in four weeks should inhibit tumor growth and not give rise to delayed radionecrosis. Ingraham and Matson[9] used a tumor dose of 3,000 r (treatment time not specified). Bray *et al.*[5] felt 4,000 r in twenty-eight days to be a desirable level. With orthovoltage (200–240 kv. peak) roentgen rays we have delivered 3,500–4,000 r tumor dose in four weeks with no known instances of radionecrosis.

In recent months we have been using higher energy radiation sources such as cobalt 60. The well known skin-sparing and decreased bone absorption effects as well as increased depth dose may prove advantageous in the treatment of these tumors. Because of the evidence of better results with higher tumor doses, 4,500–6,000 r has been delivered with increased protraction and fractionation to avoid radionecrosis.

Attention must be given to the use of sufficiently large fields. The irradiated volume should be generous as many of these tumors extend considerably beyond the pons proper. Buckley[6] found extrapontine extension in 21 of 25 autopsied cases of pontine glioma.

Bouchard,[4] while emphasizing the superiority of a *single* continuous protracted course of treatment, occasionally re-treats a

patient with reactivation if a period of six months has elapsed since the initial treatment *and* if a good response was previously obtained. Bray *et al.*[5] found re-treatment to be valueless if there was no response to the initial therapy. Of 7 re-treated patients in our series, 4 showed improvement (usually less than that following the initial treatment).

Bouchard[4] feels that most brainstem tumors are radiosensitive to varying degrees, although their curability is low, perhaps more because of the vital site of the tumor than because of histologic type. While pontine gliomas may not be radiocurable because of their strategic location and the radiovulnerability of the brainstem, radiation therapy nonetheless plays an important role in the management of these tumors.

CONCLUSIONS

1. Pontine gliomas are most common in childhood and are characterized by multiple cranial nerve and pyramidal tract involvement.

2. The clinical course is usually rapidly progressive, and the majority of patients survive less than one year after diagnosis.

3. Four of 30 patients treated with roentgen therapy survived five years or longer and enjoyed useful active lives.

4. Twenty of 30 treated patients showed definite improvement following roentgen therapy.

5. It is suggested that 4,000 r in four weeks is a desirable tumor dose, using conventional radiation. Below this level response is less frequent and less marked.

6. Higher energy radiation sources such as cobalt 60 along with higher tumor doses (using greater protraction and fractionation) give promise of improved results.

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VOL. 86, NO. 4

A SIMPLE PITUITARY LOCALIZER FOR RADIATION THERAPY*

By JACOB I. FABRIKANT, M.D.,† THOMAS B. COCKEY, M.D., *and* PAUL N. GOODWIN, PH.D.
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IT IS desirable, in conventional orthovoltage therapy, to use multiple ports for the treatment of pituitary adenomas to permit delivery of a satisfactory tumor dose without severly compromising the hair, skin, and underlying tissues in the path of any one port. This report describes a simply designed pituitary localizer (Fig. 1) which enables the therapist properly to apply multiple wax seatings to a head cast in such a way that the central ray through each seating will pass through the sella turcica.

The localizer consists of two aluminum rods joined as a T-bar in the center of one, forming a movable angle rule which may be immobilized with a wing nut. The horizontal bar is calibrated in centimeters from the center and extends to 9 cm. to each side. Screw-locking rings aid to center the wing nut in the head cast and lock the horizontal bar in position. The vertical bar is calibrated in centimeters from the wing nut and is marked from 6 to 15 cm. An aluminum disk, 6 cm. in diameter, slides perpendicularly onto the vertical rod. A waxed disk of pliable cardboard is placed between the aluminum disk and the wing nut. The localizer is readily dismantled into its component parts.

The position of the sella turcica is located roentgenographically by adjusting the head in a true lateral position and directing the central ray horizontally through a point 2 cm. anterior to and 2 cm. above the external acoustic meatus. A 5 cm. cone will include a generous area surrounding the sella turcica on the port roentgenogram.

When the lateral position of the sella turcica is ascertained, the point of the central ray on either side of the head is marked. The head cast is then constructed, bringing the plaster of paris somewhat below the marks (Fig. 2). Three additional ports are marked on the outside of the case and cut out with a 2 inch circle cutter. The horizontal rod of the localizer is passed through small side holes, and the wing nut is positioned in the center of the cast by the screw-locking rings. The vertical rod is passed through the open ports and joined to its mate with the washer and wing nut. Warm wax seatings are placed into the open ports (backed by the waxed cardboard) and pressed perpendicular to the vertical rod with the sliding lubricated aluminum disk. When the wax seatings are sufficiently hardened, the localizer is dismantled and removed.

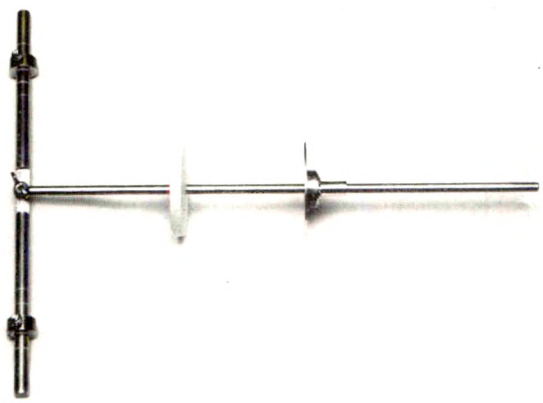


FIG. 1. Pituitary localizer.

A closed 5 cm. cone applicator is used during therapy. Its end is brought to the wax seatings and positioned perpendicular to the wax surface. The central ray will now replace the position of the vertical bar and will pass through the sella turcica (position of the wing nut), no matter at which position the port was previously marked on

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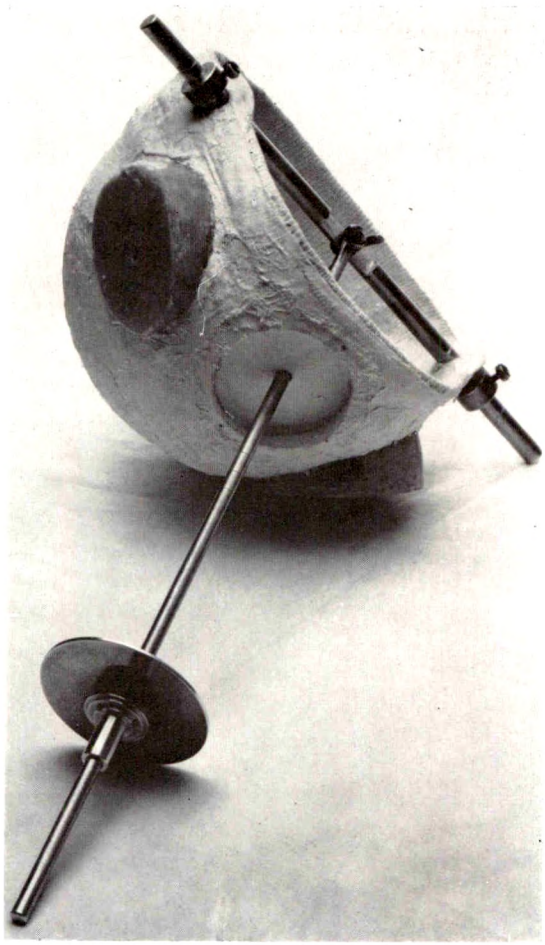


FIG. 2. Position of pituitary localizer in plaster head cast.

the surface of the cast. This has been verified with port localization roentgenograms.

Because the position of the wing nut represents the point at which a predetermined number of ports will intersect within the head, it is therefore possible to use the localizer for lesions which are not necessarily in the median plane. This may be accomplished by placing the wing nut in t general position of the lesion and shiftir the screw-locking rings to secure the loca izer in the desired position. The subseque steps to design the head cast and wax sea ings remain the same.

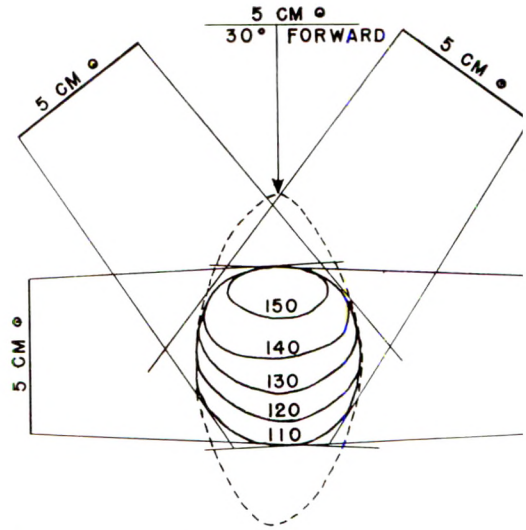


FIG. 3. Isodose distribution utilizing five 5 cm. fiel 250 kvp. deep roentgen-ray therapy unit.

SUMMARY

1. A simple and reliable pituitary loca izer for radiation therapy is described.

2. It is used to position multiple por for treatment of the pituitary gland wh a head cast technique is employed.

3. It may be modified to permit directi of the central beam to any small volun within the cranial vault.

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VOL. 46, NO. 4

CONTRAST EXAMINATION OF LARYNX AND PHARYNX*

ACCURACY AND VALUE IN DIAGNOSIS

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IF THE treatment of laryngeal or laryngopharyngeal cancer required total laryngectomy regardless of location, size or extent of the tumor, accurate preoperative appraisal of these tumors would be unnecessary. However, with the advent of surgical and radiation therapy procedures by use of which laryngeal function can be preserved in cases of glottic or selected supraglottic and hypopharyngeal tumors, such evaluation becomes mandatory.

A roentgenographic examination proves to be worthwhile only if it can produce consistent and valuable diagnostic information. By contrast roentgenography of the larynx and hypopharynx, tumor masses of these structures can be accurately defined as to location, size and extent. Functional impairment of these structures can be demonstrated. The method is direct, simple, accurate and safe. It can be performed with simple equipment, gives little radiation to the patient and examiner, and takes no more time than a gastrointestinal series. No other method of roentgen examination of this region has been shown to be equally accurate.

Laryngography is not a screening procedure but supplements the otolaryngologist's examination and biopsy. It is more direct and more explicit than laminagraphy or combined laminagraphy and barium swallow studies. No cine-equipment is required to perform a physiologic examination.

Since radiation therapy is the treatment of choice in mobile glottic lesions, a true estimate of mobility and subglottic extent can be graphically recorded by laryngography and glottic lesions can be properly staged. It is also possible by these records to show response of the tumor to irradiation and the functional result after therapy (Fig. 1, *A* and *B*).

TECHNIQUE

The procedure is essentially the same as reported by Powers, McGee and Seaman.[5] The patient is prepared with nembutal and atropine. A topical anesthetic is sprayed into the pharynx and dropped into the larynx. If the patient is in the hospital, 10 per cent cocaine is used; otherwise 1 per cent pontocaine is applied. Ten to twenty cubic centimeters of oily dionosil are dropped slowly over the tongue during quite inspiration. Frontal and lateral spot roentgenograms are made during nasal inspiration, phonation, modified Valsalva and true Valsalva maneuvers. The examination is made before biopsy is done so that edema will not falsely distort the anatomy.

This procedure is not accompanied by any morbidity; rarely, apprehension of the patient prevents the examination from being performed. All of the larynx and hypopharynx can be visualized at one time in one examination. It is direct as opposed to laminagraphy where faulty technique and lack of air contrast may result in errors in interpretation. The method is superior to a barium swallow examination for the hypopharyngeal region where the fleeting passage of the barium bolus is in contrast to the persistence of opacification in laryngograms. Since spot roentgenograms are taken

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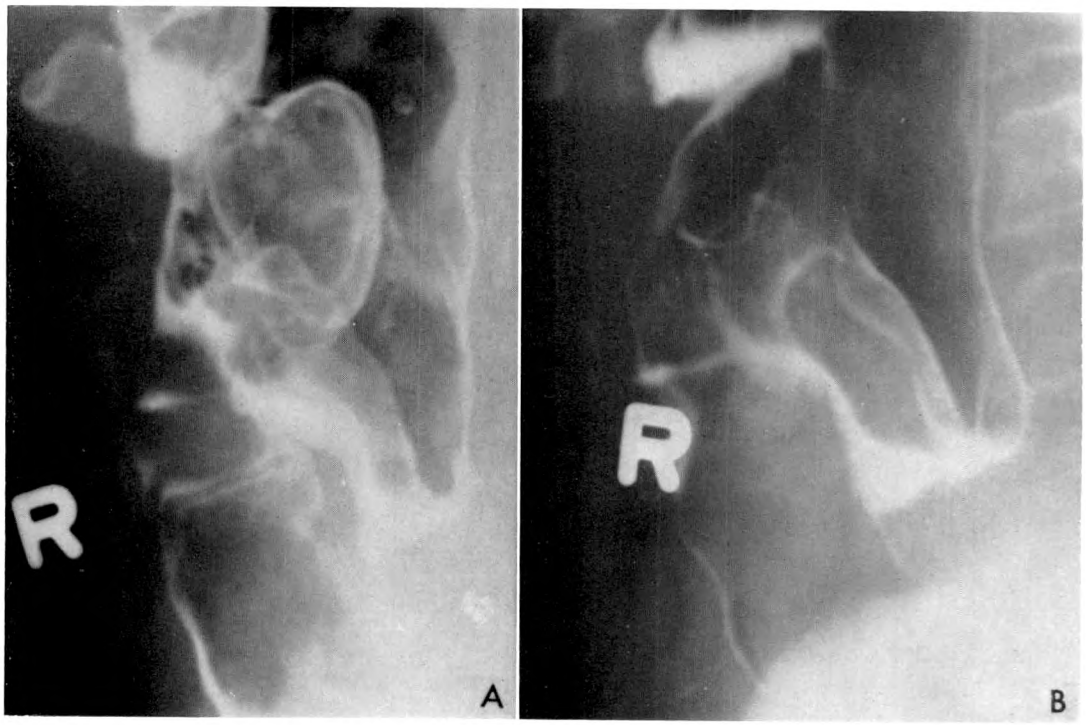


Fig. 1. (*A*) Initial laryngogram revealing a large tumor of the anterior wall of the pyriform sinus. (*B*) Laryngogram four years after therapy demonstrating the response to irradiation with disappearance of the tumor.

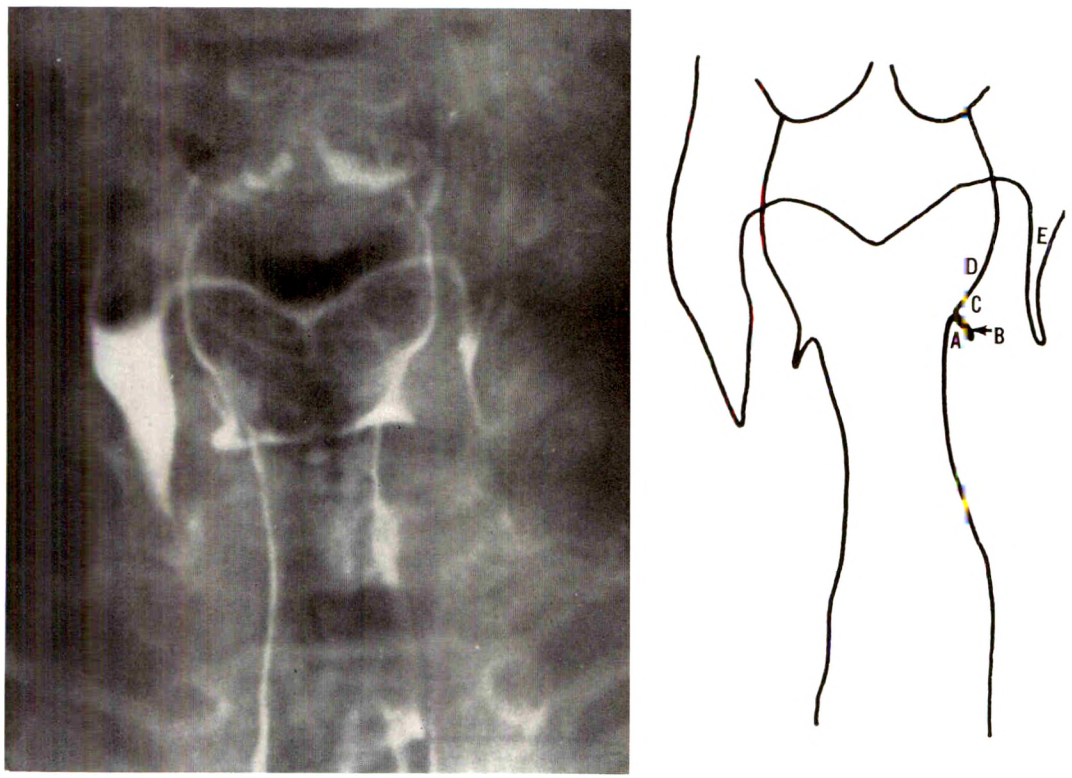
at the maximum excursion of the different maneuvers, this is a definite functional examination and in our study the quality of the laryngograms proved superior to that of cineroentgenographic studies.

NORMAL ROENTGEN ANATOMY

All of the structures of the larynx and pharynx are outlined by contrast medium and air. The normal roentgen anatomy has been carefully described in the original article[5] but several points should be reemphasized: (1) in nasal inspiration the cords are retracted and usually not seen (Fig. 2); (2) the true and false cords and vestibule are symmetric (Fig. 3); (3) the angles of the true cord that subtend with the trachea in the frontal and lateral projections are sharp, approaching a right angle; (4) during Valsalva maneuver, air and contrast medium are forced against the undersurface of the true cords, thus accurately defining the beginning of the infraglottic space and any masses that may be present there (Fig. 4); and (5) the lateral wall of the pyriform sinus may be slightly asymmetric, the medial wall usually is not. Lack of change of the pyriform sinus in the different maneuvers indicates infiltration.

CLASSIFICATION AND PATHOLOGIC SIGNIFICANCE OF LOCATION AND SIZE OF THE PRIMARY LESION

Classification of laryngeal lesions differs in various sections of the country and over the world. Recently, McGavran, Bauer and Ogura[1] have reviewed the specimens of laryngeal cancers of cases where *en bloc* total or supraglottic subtotal laryngectomy with incontinuity neck dissection was performed between 1950 and 1959. No case with prior radiation treatment or other surgical intervention has been included. The proposed classification (Fig. 5) based on pathologic data is: (1) glottic—cancers limited to the true cord; (2) infraglottic—cancers of the subglottis and glottis; (3)



IG. 2. Laryngogram and tracing showing that the true cords (A) and false cords (C) are retracted with the true cords almost obliterating the ventricle (B). A thin line of contrast material outlines the ventricle, the posterior portion of which lies laterally. The pyriform sinus is seen (E). (Nasal inspiration—frontal view.) (Reproduced by permission from *Radiology*.)

upraglottic—cancers involving the false ord, fixed or free portions of the laryngeal urface of the epiglottis; and (4) transglotc—cancers that cross the ventricle thus nvolving two or more of the above sites. The rare ventricular tumors are included in his group.

This classification is based on areas of nvolvement and does not include the hypoetical extrapolation from size and locaon as to the point of origin. It is based on here tumor is rather than a supposition s to where it began. The glottic, infraglotc and supraglottic types are similar in efinition to that used by Pietrantoni and ior.[4] The value of this classification is the act that lesions are separated according to he two major divisions of lymphatic drainge.

Of 96 patients studied, it was noted that: 1) there was a progressive increase in metastatic incidence from glottic to infraglottic, to supraglottic to transglottic lesions—0, 19, 33 and 52 per cent, respectively. The metastatic rate of the transglottic group represents the addition of the infraglottic and supraglottic lymphatics, confirming the expected results derived from theoretic considerations of the lymphatic drainage of the larynx (Table I); (2) the transglottic group yielded a higher incidence of both clinically apparent and inapparent metastases. The rate for inapparent metastases for the infraglottic group was 22 per cent, the supraglottic group 4 per cent and the transglottic group 31 per cent (Table II); (3) supraglottic and infraglottic cancers larger than 2 cm. and of moderate or poor differentiation also presented with a high incidence of metastases (15/30) (Table III). Cancers of any size that were well differentiated in these two locations, or

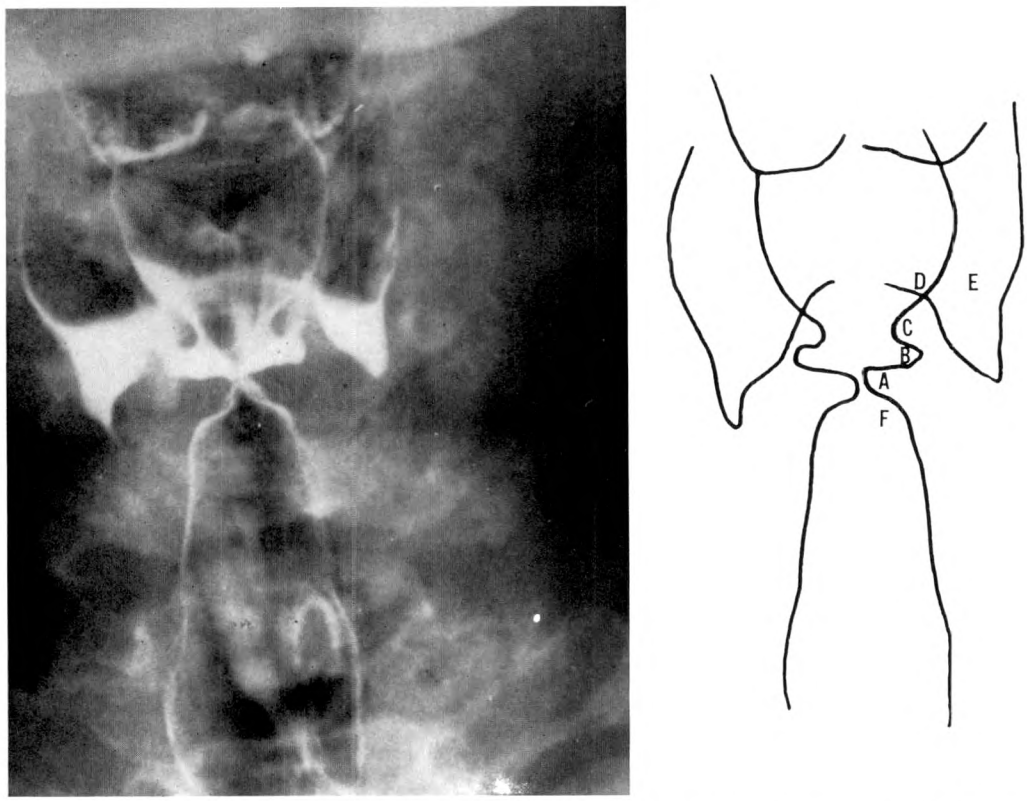


Fig. 3. Laryngogram and tracing showing that the true cords (A), the false cords (C) and vestibule (D) ar symmetric. The angle between the true cord and the trachea (infraglottic space—F) is sharp, approachin a right angle. The pyriform sinus (E) has changed in shape from that seen on the inspiration laryngo gram. B represents the ventricle. (Phonation—frontal view.) (Reproduced by permission from *Radiology*

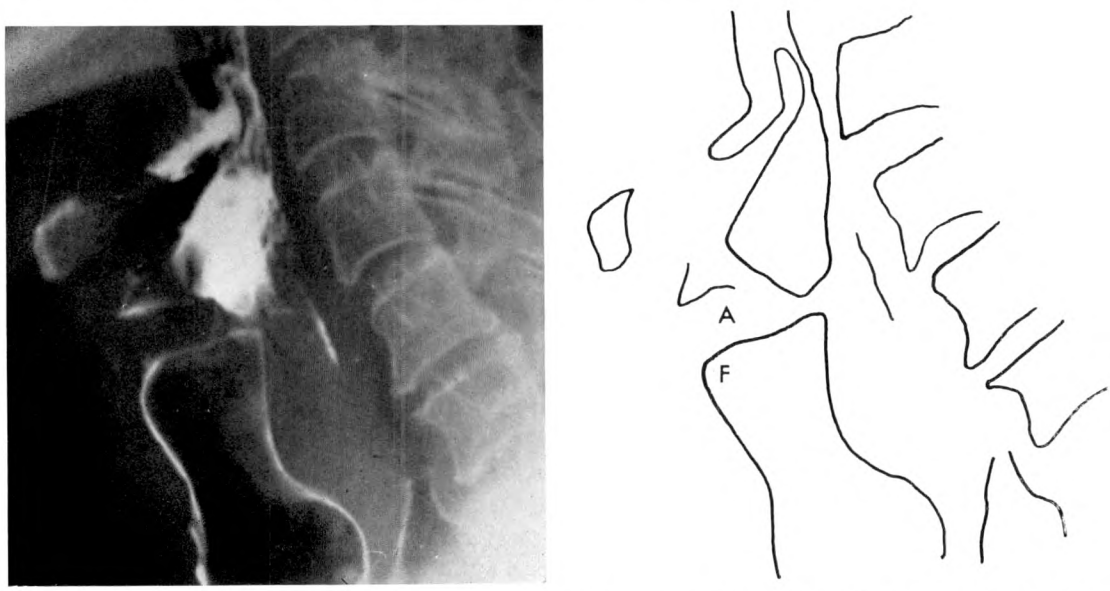


Fig. 4. Laryngogram and tracing showing air and contrast medium force against the inferior margins of th closed cords (A), which are now in the horizontal position thus accurately defining the infraglottic spac (F). (Valsalva maneuver—lateral view.) (Reproduced by permission from *Radiology*.)

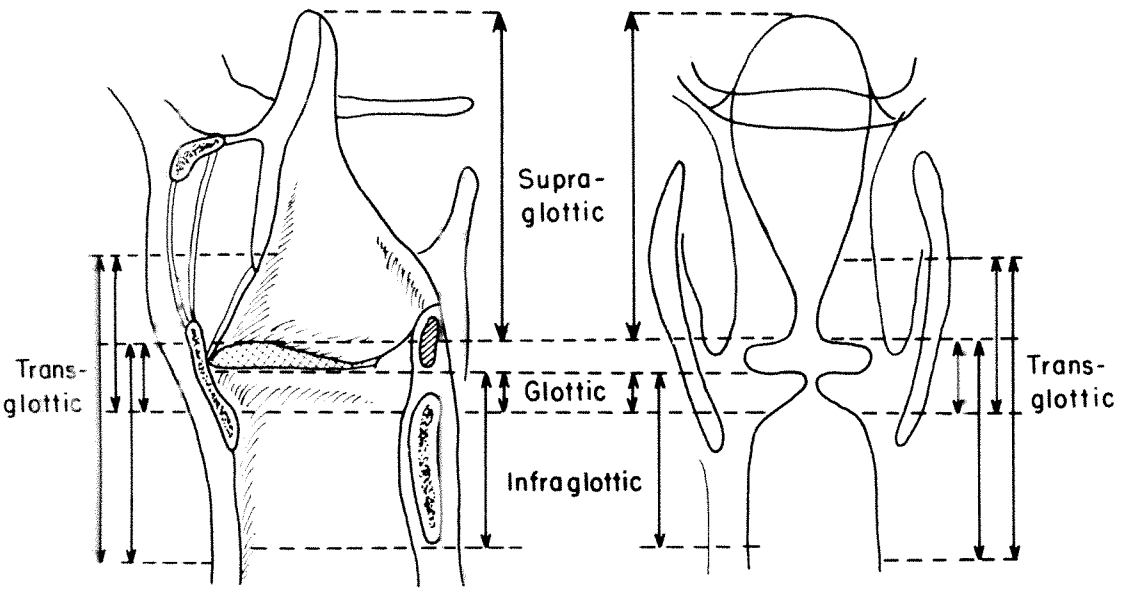


FIG. 5. Diagram showing the classification of laryngeal tumors. (Reproduced by permission from *The Laryngoscope*.)

those of 2 cm. or less and moderately or poorly differentiated, provided a low incidence of metastases to the neck (2/20); (4) of 23 patients with supraglottic or transglottic lesions shown to have cervical lymph node metastases, 48 per cent had proved positive lymph nodes in the contralateral side of the neck on follow-up surgery.

Thus, cases of laryngeal cancer can be separated into groups of high and low metastatic incidence rates by using preoperative information about the site, size and biopsy differentiation of the primary lesion and clinical evaluation of the cervical lymph nodes.

METHOD OF STUDY

Since this study was designed to appraise the diagnostic accuracy of laryngography, it was necessary to document the clinical, roentgenographic and pathologic data separately. This was done on 99 consecutive patients from 1957–1959 who had laryngographies and subsequent surgery, with sur-

TABLE I

METASTATIC INCIDENCE IN 96 CASES OF LARYNGEAL CANCER TREATED BY EN BLOC LARYNGECTOMY AND RADICAL NECK DISSECTION AND ITS RELATIONSHIP TO THE SITE OF LESION
(McGavran *et al.*[3])

Site	No. of Cases	Cases with Positive Lymph Nodes	Per Cent
Glottic	5	0	0
Infraglottic	27	5	19
Supraglottic	39	13	33
Total (a)	71	18	
Transglottic (b)	25	13	52
All Sites	96	31	32

$\chi^2 = 6.02$; p (a) = (b) 0.02.

TABLE II

METASTATIC INCIDENCE IN 68 CASES OF LARYNGEAL CANCER TREATED BY EN BLOC LARYNGECTOMY AND ELECTIVE NECK DISSECTION AND ITS RELATIONSHIP TO THE SITE OF THE LESION
(McGavran *et al.*[3])

Site	No. of Cases	Cases with Positive Lymph Nodes	Per Cent
Glottic	4	0	0
Infraglottic	23	5	22
Supraglottic	25	1	4
Total (a)	52	6	
Transglottic (b)	16	5	31
All Sites	68	11	16

$\chi^2 = 3.5$; p (a) = (b) 0.06.

TABLE III

SIZE AND CELLULAR DIFFERENTIATION OF THE RESECTED SPECIMEN AND METASTATIC INCIDENCE IN 96 CASES OF LARYNGEAL CARCINOMA TREATED BY EN BLOC LARYNGECTOMY AND RADICAL NECK DISSECTION
(McGavran *et al.*[3])

	No. of Cases	No. of Cases with Metastases	χ^2 P, (a) = (b)
Size			
2 cm. or less (a)	29	4 (14%)	6.5 <0.02
Larger than 2 cm. (b)	67	27 (40%)	
Differentiation			
Well	9	1 (11%)	
Moderate	46	10 (22%)	
Total (a)	55	11	
Poor (b)	41	20 (49%)	8.9 <0.01

gical specimens available for comparison. Six of 13 patients with glottic lesions had hemilaryngectomies and the remainder had total or subtotal laryngectomies, all with *en bloc* neck dissection.

The laryngograms were reviewed by the radiologists without regard to previous interpretation and classification or knowledge of clinical data. Noted were: (I) the sites of the lesions (1. glottic; 2. infraglottic; 3. supraglottic; 4. transglottic; and 5. pyriform sinus); (II) the area of involvement (1. the size; 2. the structures involved; 3. whether adjacent structures were invaded or free; 4. the superior-inferior extent of the tumor; 5. the mobility of the cords; 6. involvement of the anterior commissure and across the midline; and 7. involvement of the pyriform sinus, the aryepiglottic fold and the base of the tongue). The cases were then placed into the various classifications. Comments were made as to whether radical excision in supraglottic or pyriform sinus lesions was necessary or whether a "conservation of function" operation could be performed (supraglottic subtotal or transhyoid partial laryngopharyngectomy).

The clinical and direct laryngoscopic observations were then recorded from the hospital records on a master sheet. These findings represented the combined notes of the residents and the attending surgeon and the same criteria for accuracy and error were used as for the evaluation of the laryngograms. Accuracy was verified by correlating the findings with the gross surgical specimens and photographs. Errors were listed whenever the laryngographic interpretations resulted in an erroneous classification.

RESULTS

During the 1957–1959 study period, seven laryngograms made of laryngeal cancer patients were discarded for the following reasons: poor coating, 2 cases; poor quality or insufficient views, 2 cases; edema and distortion as a result of irradiation, 2 cases; and insufficient coating and poor airway in a tracheotomized patient. Four laryngograms could not be located. It was impossible to obtain laryngograms on 2 patients because of uncooperativeness. Laryngograms of 25 other patients were not included since irradiation was the treatment of choice, and therefore no specimen was available for examination. Ten cases had far-advanced cancer and surgery was not considered. Twenty patients with laryngeal cancers underwent surgery without laryngography. In 3 patients laryngograms were made but neither surgery nor roentgen-ray therapy was undertaken. Thus the total number of cases excluded was 71.

The remaining 99 cases of a total of 170 cases of all forms of laryngeal cancer observed during this three year period had a satisfactory evaluation and were used for the present study.

The accuracy of laryngography proved to be high (Table IV), 92 per cent as contrasted to 78 per cent using conventional clinical appraisal. The majority of errors occurred in the infraglottic group. This was due to an enlarged true cord and infraglottic mass (which was fixed most of the time) impressing and almost obliterating the ventricle. Because of the incorrect interpretation of false cord involvement, these cases were classified as transglottic lesions. In only 1 case was infraglottic ex-

TABLE IV

COMPARISON OF THE ACCURACY OF CLINICAL EXAMINATION AND DIRECT LARYNGOSCOPY WITH LARYNGOGRAPHY

Site	Diagnosis	Clinical Examination and Direct Laryngoscopy	Laryngography	Confirmative Surgical Pathology
Glottic	Correct	12	12	13
	Incorrect	1	1	
Infraglottic	Correct	7	9	14
	Incorrect	7	5	
Supraglottic	Correct	22	28	29
	Incorrect	7	1	
Transglottic	Correct	10	16	16
	Incorrect	6	0	
Pyriform Sinus	Correct	26	26	27
	Incorrect	1	1	
Total	Correct	77 } 22%	91 } 8%	—
	Incorrect	22 }	8 }	99

tension missed on the laryngogram. With continued refinement in technique, it should be possible to decrease the error caused by the misinterpretation. Other errors of interpretation were extremely low and are to be expected.

Clinical classification in certain cases of laryngeal and pharyngeal lesions is difficult. Bulky supraglottic tumors are airway problems and the precise lower margins cannot be determined accurately. In this group, freedom of involvement of the true cord can be seen on laryngograms since the lower margins of the neoplasm are defined. Bulky tumors of the false cords that overhang the true cord can also be precisely visualized on laryngograms. Clinically, such tumors are often mistakenly considered to involve the true cord. Tumor crossing the midline was correctly evaluated by laryngography in every case in the supraglottic, infraglottic and transglottic lesions. There was a high accuracy index for pyriform sinus lesions both from the clinical and roentgenographic standpoints.

By laryngography the size of the tumor can be determined for all sites within a mean variation from 0.3–0.6 cm. depending upon the tumor site (Table v), and frequently the actual tumor size can be correlated with the laryngogram. This is impossible by laryngoscopy. The size of tumor, degree of differentiation and location of the lesion have a direct relationship to metastatic spread.

Laryngography was not designed for the appraisal of lesions in the post-cricoid region, and here a barium swallow study becomes necessary. The determination of anterior commissure involvement also is difficult by contrast roentgenography, although suggestive signs may be present.

DISCUSSION

Since 1950 operative procedures less radical than a total laryngectomy have been performed on selected cases at this institution[2] (Fig. 6 and 7). These preserve the cords but are combined with a radical cervical lymph node dissection. The patients have no significant speech disturbance, and are able to swallow without as-

TABLE V

ACTUAL SIZE OF PRIMARY LESION AND LARYNGOGRAPHIC VARIATION

Site	Actual Size	Laryngographic Variation
Glottic	—	—
Infraglottic	1.3–2.6 cm.	±0.3 cm.
Supraglottic	1.0–5.0 cm.	±0.6 cm.
Transglottic	1.8–5.0 cm.	±0.4 cm.
Pyriform Sinus	1.0–6.0 cm.	±0.6 cm.

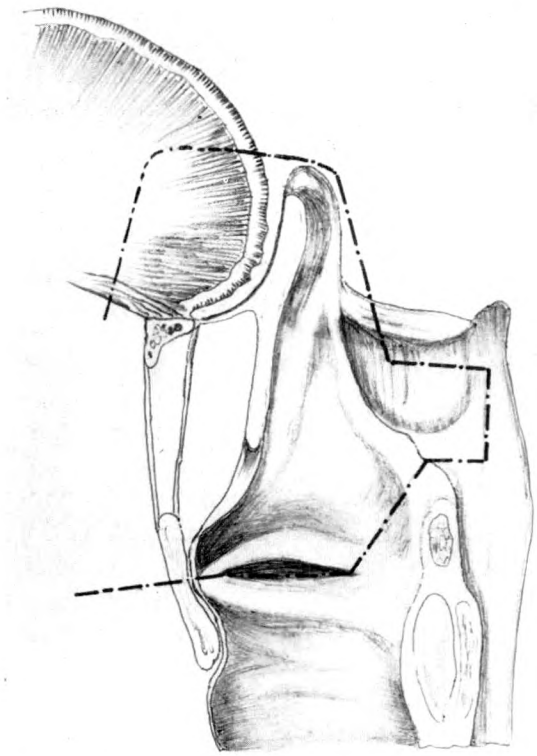


Fig. 6. Drawing showing subtotal supraglottic laryngectomy. The structures enclosed within the interrupted lines are removed, leaving the true cords intact. (Reproduced by permission from *The Laryngoscope.*)

piration (Fig. 8, *A*, *B* and *C*).[3] A one to six year follow-up on these selected cases has shown good results.

The accuracy of the radiologists in classifying supraglottic lesions was high. Out of 17 cases having supraglottic operation, 12 were noted as having wide surgical margins of safety. Examination of the surgical specimens verified this. In 5 cases, where the tumor was in the false cord area, the diagnoses and the extent of the safety margin as evaluated by laryngography correlated well with the findings at surgery. In 6 out of 12 cases in which laryngectomy and neck dissection was performed, laryngograms showed that a supraglottic subtotal operation could have been done. Examination of the surgical specimen confirmed this. The clinical preoperative appraisal was that "there was insufficient margin of safety."

The lymph node metastatic spread is quite dependent upon the location and extent of the primary lesion, its size and degree of differentiation. The time may come when prophylatic neck dissections are abandoned on patients with supraglottic carcinoma, where the metastatic rate of clinically inapparent lymph nodes is low

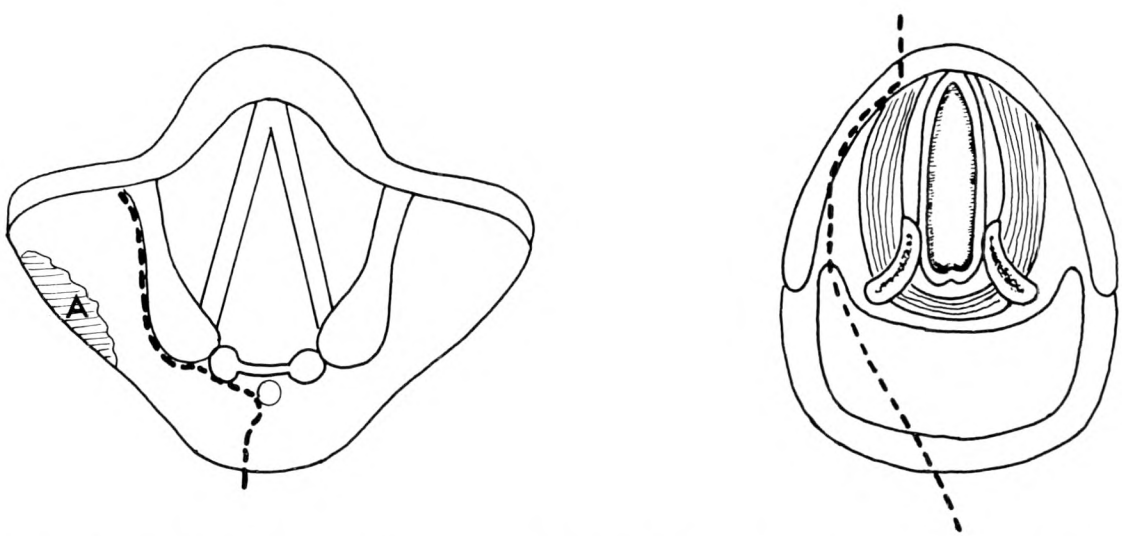


Fig 7. Drawing showing a partial pharyngectomy, by which the tumor on the lateral wall of the pyriform sinus is removed and function is preserved. (Reproduced by permission from *The Laryngoscope.*)

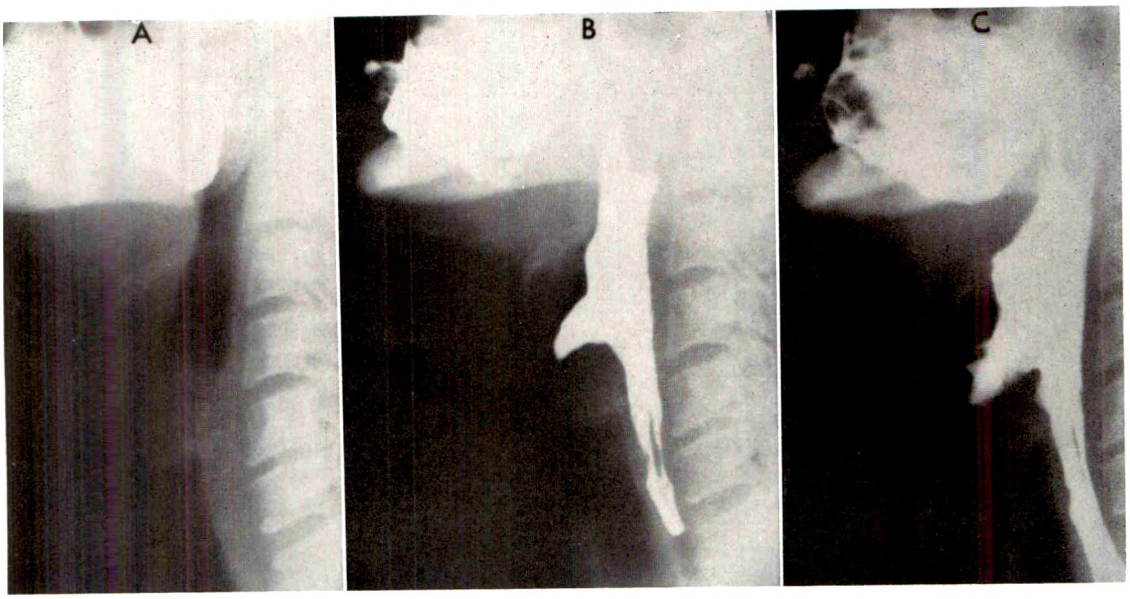


FIG. 8. Postoperative barium swallow studies. (*A*) A plain roentgenogram showing that the epiglottis is absent. (*B* and *C*) Studies showing the stages in swallowing. The barium has entered the vestibule but the cords remain closed, protecting the trachea.

and the patients might be better treated by adequate irradiation. With improved methods of selection of patients and better defined treatment factors, conservation of function falls within the scope of radiation therapy.

Clinical estimation of the extent of cancer involving the infraglottic and transglottic groups has been frequently in error. This is because the fixation of the cord masks the size of the tumor. Size and extent of subglottic involvement are difficult to appraise even with a mobile or partially paretic cord. In the transglottic group, tumors that involve and fix the false and true cords frequently obscure a large infraglottic extension. In addition, the base of the epiglottis is sometimes overlooked. In all of these situations, laryngograms have proved their value by precisely localizing and sharply delineating the lower extent of the tumor. At this institution, radiation therapy is considered the method of choice for patients with glottic cancer and mobile cords, with a resultant five year cure rate approaching 90 per cent. Involvement of the false cord and infraglottic space increases the incidence of lymph node metastases and these factors plus fixation of the cord alter the prognosis. It is felt that radiation therapy should be considered in cases of glottic lesions with a fixed cord or with infraglottic extension; however, the present trend of treatment for these lesions has been surgical. Laminagraphy, in our experience, has correlated poorly with the findings at surgery. By laryngography a baseline for future follow-up examinations can be established from which the response of the tumor to irradiation can be ascertained.

SUMMARY AND CONCLUSIONS

1. Laryngography, while not a screening procedure, has proved to be an accurate diagnostic technique in lesions of the larynx and pharynx.

2. Laryngography is a physiologic examination capable of recording variations objectively.

3. The entire anatomy of the larynx and hypopharynx can be recorded simultaneously.

4. It is a safe, simple, direct, rapid and accurate procedure.

5. By laryngography the size and location of the lesion can be determined more accurately than by clinical evaluation.

6. An analysis of data obtained from a study of total or subtotal laryngectomies with routine *en bloc* neck dissection has given us very valuable information as to certain characteristics of the primary lesion.

7. The size of the tumor, degree of differentiation and the location have a relationship to clinically apparent and inapparent cervical metastatic spread.

8. An accurate clinical classification of cancer of the larynx is necessary since the choice of therapy is governed by the probability or location of metastases.

9. A pathologic classification based on the location of the primary lesion is suggested for laryngoscopic and clinical use. Since the proposed classification indicates that there is a progressive increase in metastatic rate from glottic to infraglottic, to supraglottic, to transglottic cancers, the type of treatment to be administered can be determined.

10. The indications will be based on: (a) conservation of function by radiation therapy for early lesions of the cord; (b) larynx-sparing therapy for selected cases of supraglottic or pyriform sinus lesions; or (c) more radical operations (total laryngectomy to include neck dissection) when the inapparent metastatic rate is high.

11. Laryngograms can demonstrate graphically the response of lesions to irradiation and is an accurate documentary method of following patients after therapy.

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VOL. 86, NO. 4

LARYNGEAL PATHOLOGY ON THE CONVENTIONAL ROENTGENOGRAM OF THE CHEST*

DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE

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IN THE interpretation of routine chest roentgenograms, careful scrutiny of the air column overlying the cervical spine can prove to be a truly rewarding effort. The radiologist may be the first to recognize early carcinoma of the laryngopharynx or trachea as well as vocal cord paralysis secondary to recurrent laryngeal nerve involvement.

Earlier detection of carcinomas of the laryngopharynx, prior to the appearance of gross clinical symptomatology, can provide a greater probability for cure by surgery and/or radiation. The radiologist's early roentgenographic report of laryngeal nerve paralysis is the basis for further investigative studies to determine the etiologic factor. Attention is thus promptly directed to primary or secondary malignant disease in the neck, thorax or elsewhere. In such instances, the roentgen findings may become of paramount importance in planning appropriate clinical management of the patient.

In a study of paralyzed vocal cords which we recently completed,[12] it became apparent that the roentgen evidence was frequently overlooked by the radiologist during roentgenographic and fluoroscopic examinations not specifically related to the larynx—such as studies of the cervical spine and ribs, esophagus and chest, both conventional and laminagraphic. In many of these instances, the attending physician was entirely unaware of the laryngeal pathology. In our department today, patients are promptly summoned for indirect mirror examination of the larynx as soon as abnormalities of the cervical air column are recognized on routine roentgenologic examinations.

In the interpretation of the visualized larynx on routine roentgen study, the radiologist must first determine whether the exposure was made during inspiration or expiration. The roentgen appearance of the larynx or glottis differs greatly in these two phases. In our recent communication,[12] we have described in detail these findings during laminagraphic examination of the vocal cords. It is striking how well these can be visualized on the conventional chest roentgenogram.

In inspiration (Fig. 1, *a* and *b*) the glottic aperture is wide, with no visualization of the ventricles; in expiration, the glottis is reduced to a narrow slit, as in phonation, and the ventricles are filled with air (Fig. 1, *c* and *d*). Usually, when the roentgenographic exposure is to be made, the subject is told to take a deep breath and hold it; or to take a breath, let it out and then hold it. If the exposure is made during any part of inspiration, the roentgenogram will show a wide glottis (Fig. 1, *a* and *b*). If the patient is at the termination of the inspiratory phase or at the beginning of expiration, he will suddenly stop his breathing and, in addition, may bear down slightly, thereby carrying out a modified Valsalva maneuver and the roentgenogram will show the vestibule, ventricles, glottis and trachea (Fig. 1, *c* and *d*).

Among the following illustrative cases there are 2 patients with carcinoma of the right vocal cord and 3 patients with paralyzed vocal cords due to recurrent laryngeal nerve involvement by metastatic mediastinal disease.

REPORT OF CASES

CASE 1. A sixty-seven year old white male

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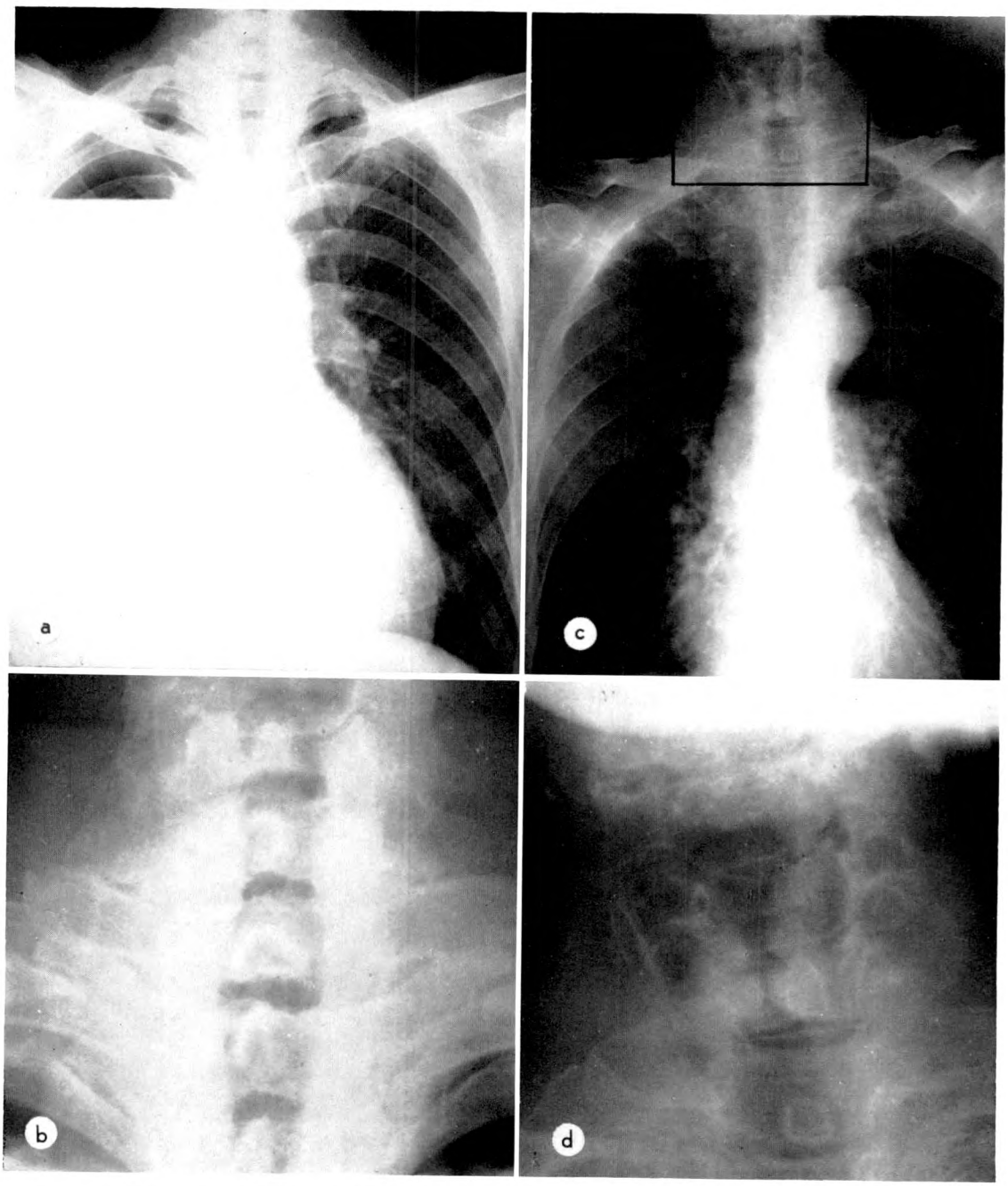


Fig. 1. (*a* and *b*) In inspiration. (*c* and *d*) In expiration. Normal anatomy of the laryngopharynx during the respiratory phases.

was admitted because of hoarseness. The admission chest roentgenogram (Fig. 2*a*) showed marked asymmetry of the glottis and a fixed right vocal cord was suspected. The air column is shown in Figure 2*b* in the marked zone. The roentgenogram was taken in inspiration and the fixed right vocal cord is very apparent. Direct laryngoscopy showed a fixed right vocal cord which was completely covered with an exophytic granular mass which involved the right ventricle and extended to the anterior commissure and the left vocal cord as well. The total laryngectomy specimen (Fig. 2*c*) shows the entire vocal cord to be replaced by epidermoid

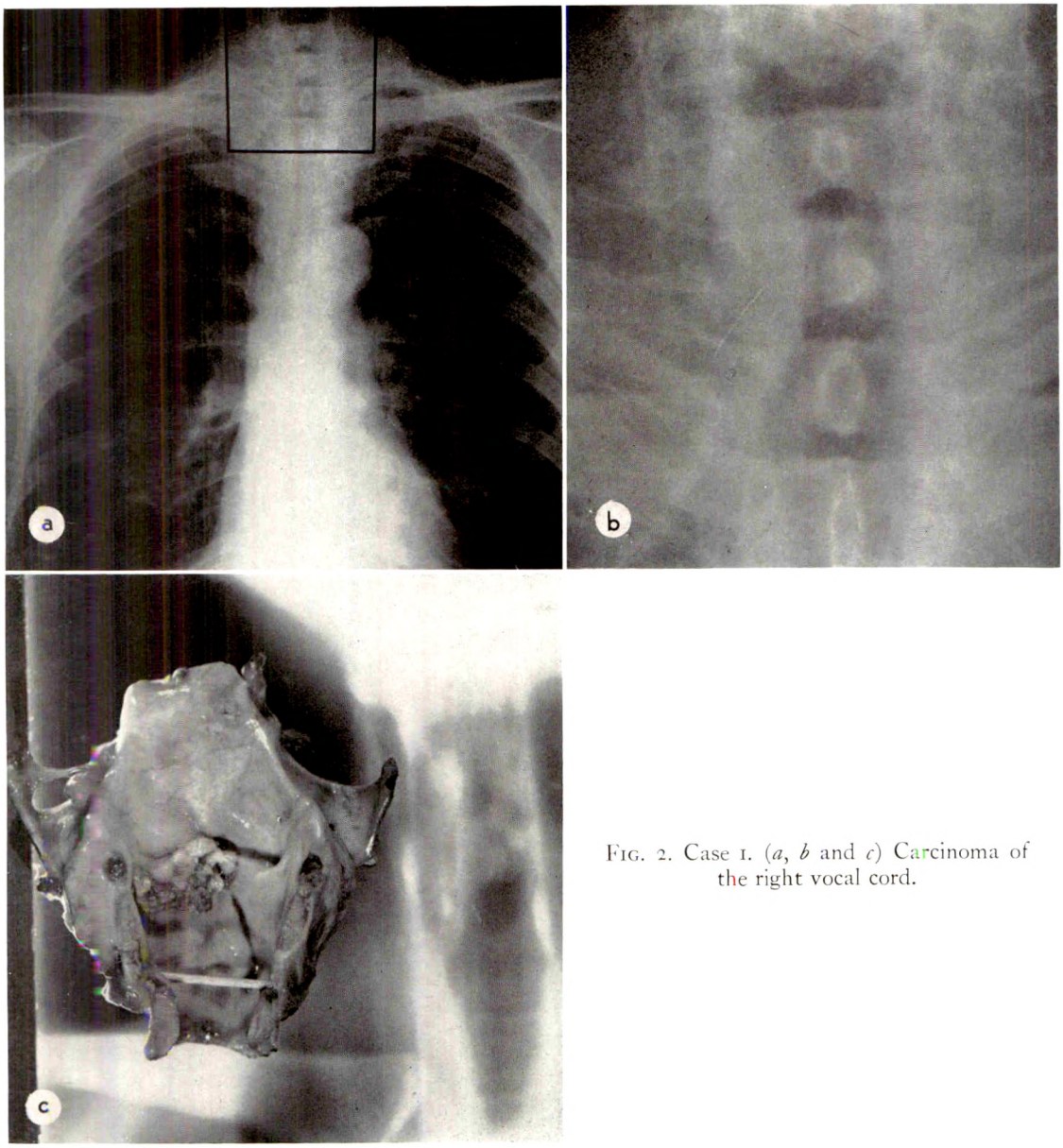


Fig. 2. Case I. (*a*, *b* and *c*) Carcinoma of the right vocal cord.

carcinoma which has extended beyond the anterior commissure to the left vocal cord. Adjacent to the specimen is a laminagram made during phonation showing poor filling of the right pyriform sinus, asymmetry of the lower part of the vestibule, incompletely filled and slightly elevated right ventricle, fixation of the right vocal cord, slightly widened glottis, and irregular left vocal cord. These roentgen findings are diagnostic of a carcinoma of the right vocal cord.

Case II. A seventy-two year old male was admitted because of pain on swallowing and hoarseness. Figure 3*a*, which is part of an esophagram, reveals obvious asymmetry of the glottis and a fixed right vocal cord. Figure 3*b*, a magnification of the marked zone shown in 3*a* during inspiration, demonstrates marked irregularity of the right vocal cord. Figure 3*c*, a laminagram taken during phonation, shows no aeration of the pyriform sinuses. The vestibule is irregular in its inferior portion and poorly filled; the ventricles are small and poorly outlined; the glottis is small and displaced to the left; the right vocal cord is irregular, but the left vocal cord is normal. These roentgen find-

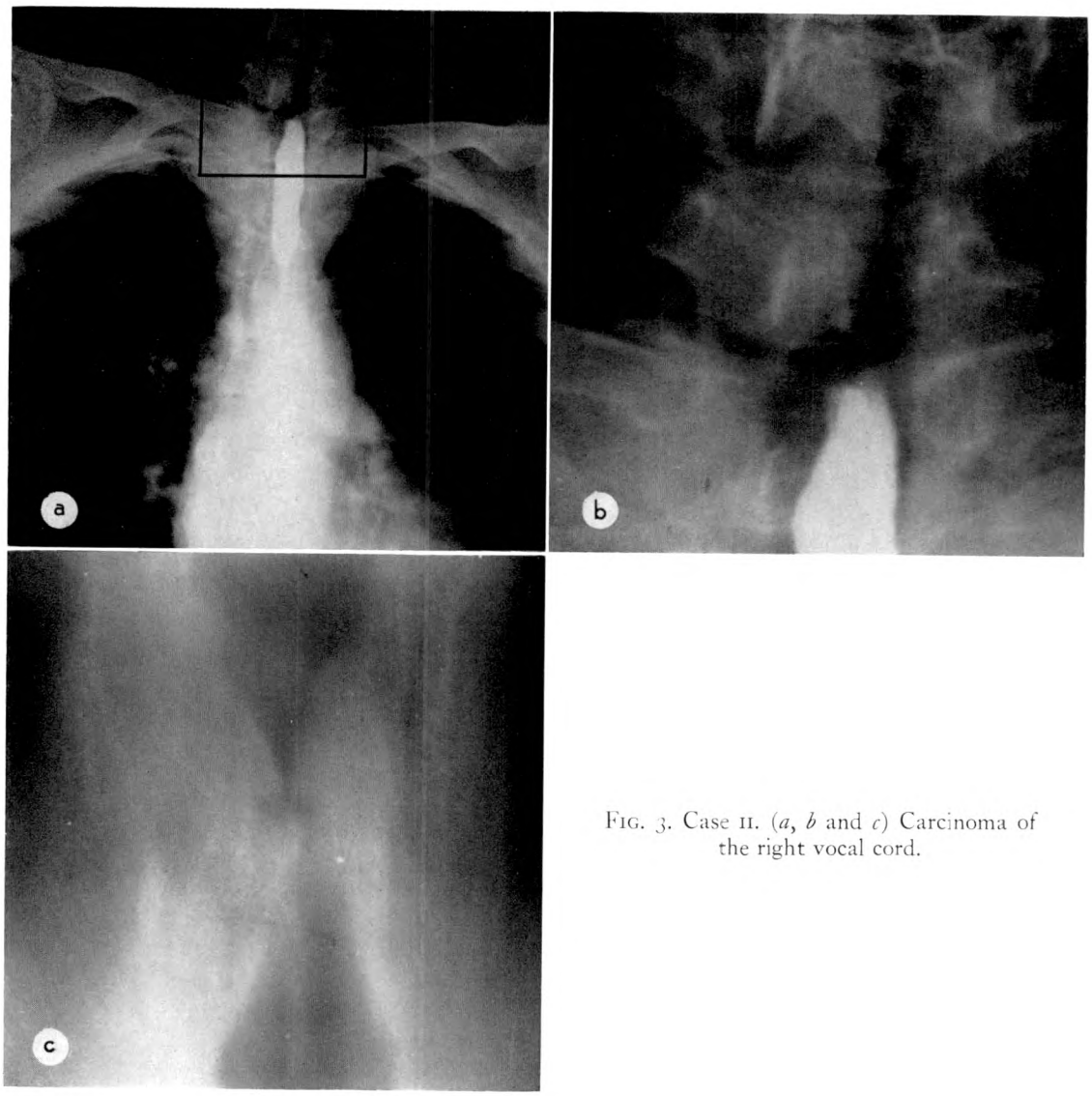


FIG. 3. Case II. (*a*, *b* and *c*) Carcinoma of the right vocal cord.

ings indicate a carcinoma of the right vocal cord. Direct laryngoscopy showed an epidermoid carcinoma in the right tonsillar region extending inferiorly along the right lateral and posterior pharyngeal wall to the right pyriform sinus and cricopharyngeus muscle. The right vocal cord was completely involved with tumor and was fixed at the midline.

CASE III. A sixty-two year old male was admitted because of dysphagia. Figure 4*a* was taken shortly after barium studies of the esophagus were carried out. There is retained contrast material within a dilated upper third of the esophagus. The narrowed segment of a constricting neoplasm in the esophagus is seen above the aortic arch. The air column of the larynx is that seen in quiet respiration and shows marked asymmetry, indicating a hypertrophied right vocal cord and paralyzed left vocal cord. Figure 4*b*, a laminagram in phonation, shows incomplete aeration of the lower part of the left pyriform sinus, asymmetry of the lower part of the vestibule, a dilated left ventricle, a normal right ventricle, a glottis displaced slightly to the left and a hypertrophied right vocal cord. These roentgen findings are diagnostic of a paralyzed left vocal cord secondary to recurrent laryngeal nerve involvement. Esophagoscopy showed, in addition to an

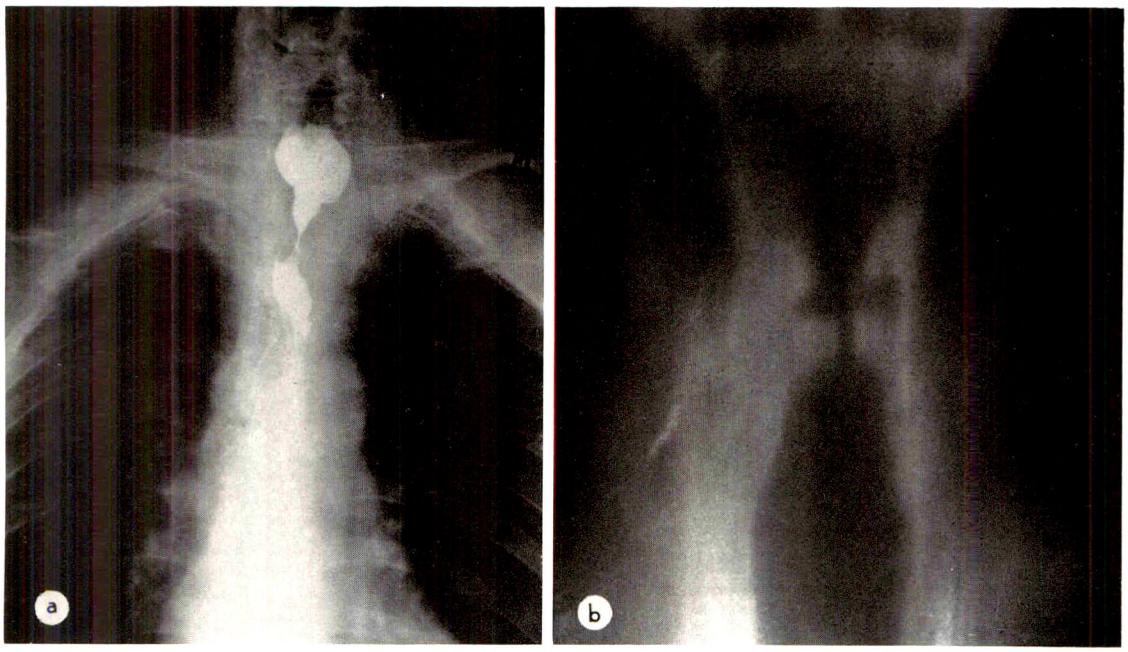


Fig. 4. Case III. (*a* and *b*) Paralysis of the left vocal cord secondary to recurrent laryngeal nerve involvement by esophageal carcinoma.

epidermoid carcinoma of the esophagus, a paralyzed left vocal cord.

Case V. A fifty-eight year old male was admitted with an unresectable bronchogenic carcinoma of the left upper lobe, proved by thoracotomy. Figure 5*a* was to have been a Bucky chest roentgenogram, but it also included the cervical spine. In addition to the left upper lobe neoplasm, the irregularity of the larynx is very distinct. Figure 5*b*, an enlargement of the marked zone in 5*a*, shows the glottis in inspiration, characterized by a paralyzed left vocal cord fixed in adduction. This was reported as such. Figure 5*c*, a laminagram in phonation, shows the pyriform sinuses and the vestibule to be poorly aerated, the left ventricle elevated and slightly larger than the right ventricle, the glottis displaced slightly to the left, and the right vocal cord hypertrophied. These findings indicate paralysis of the left vocal cord secondary to recurrent laryngeal nerve involvement.

Case 7. A seventy-two year old male had an unresectable bronchogenic carcinoma of the right middle lobe. A Bucky chest roentgenogram (Fig. 6*a*), made because of rib metastases, shows asymmetry of the glottis. An enlargement of the marked zone in 6*a* (Fig. 6*b*) shows the appearance of the glottis in inspiration, with a paralyzed left vocal cord fixed in adduction. Figure 6*c*, a laminagram in inspiration, shows air in the pyriform sinuses and vestibule, a normal right vocal cord, and a fixed and paralyzed left vocal cord. The left ventricle is filled with air and the right ventricle is partially obliterated by the mobile normal right vocal cord.

Figure 6*d* is a laminagram in phonation. Even though there is motion, the findings are characteristic of left vocal cord paralysis. Both pyriform sinuses are poorly filled with air, while the vestibule is well aerated and asymmetric in its lower portion. Both ventricles show irregular margins, but the left ventricle is larger than the right ventricle. The glottis is displaced towards the left, and the right vocal cord is hypertrophied. The roentgen findings indicate paralysis of the left vocal cord secondary to recurrent laryngeal nerve involvement.

SUMMARY

The diagnostic value of scrutiny of the air column overlying the cervical spine on routine roentgenograms of the neck and thorax is briefly discussed. The prognostic value of this observation by the radiologist

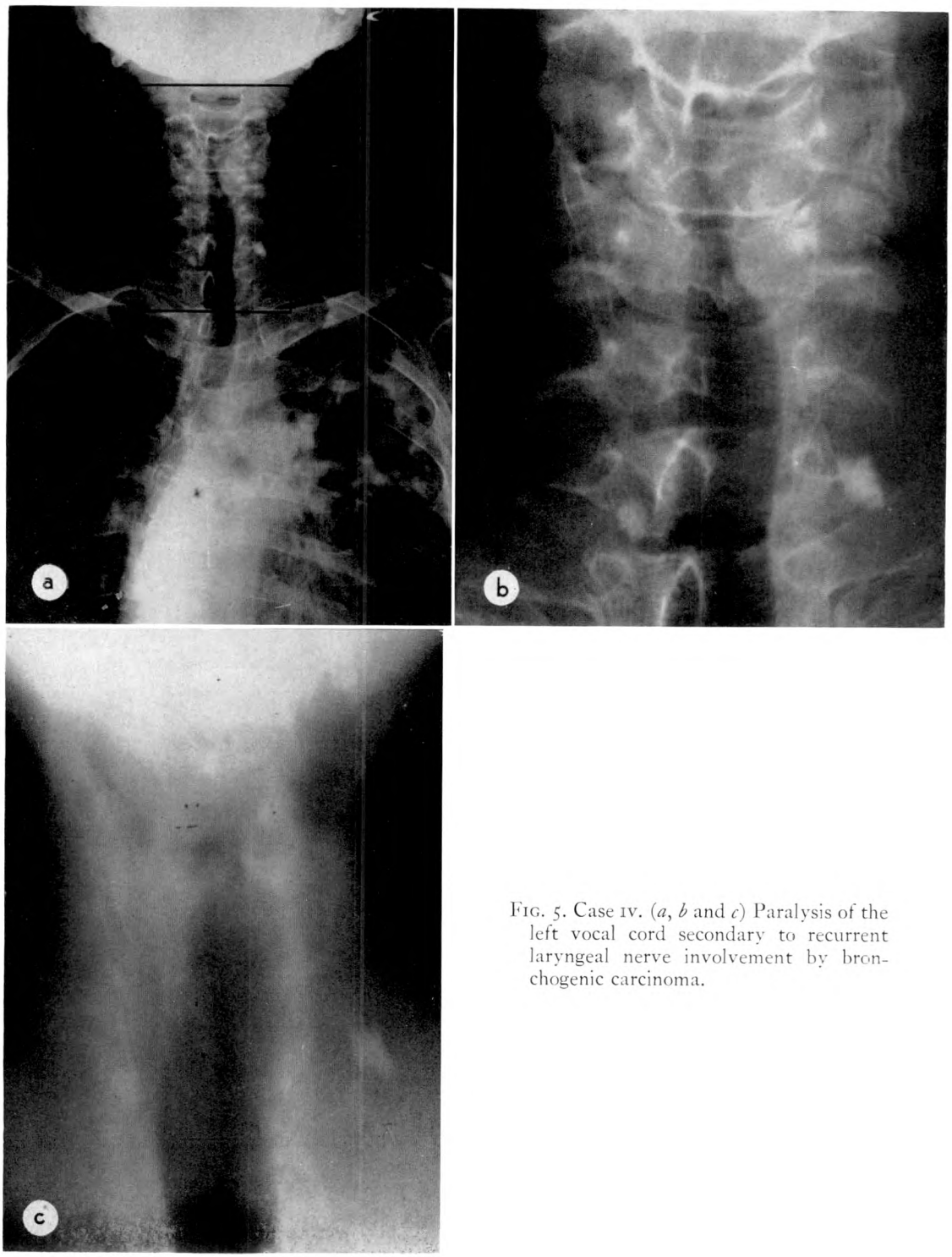


FIG. 5. Case IV. (*a*, *b* and *c*) Paralysis of the left vocal cord secondary to recurrent laryngeal nerve involvement by bronchogenic carcinoma.

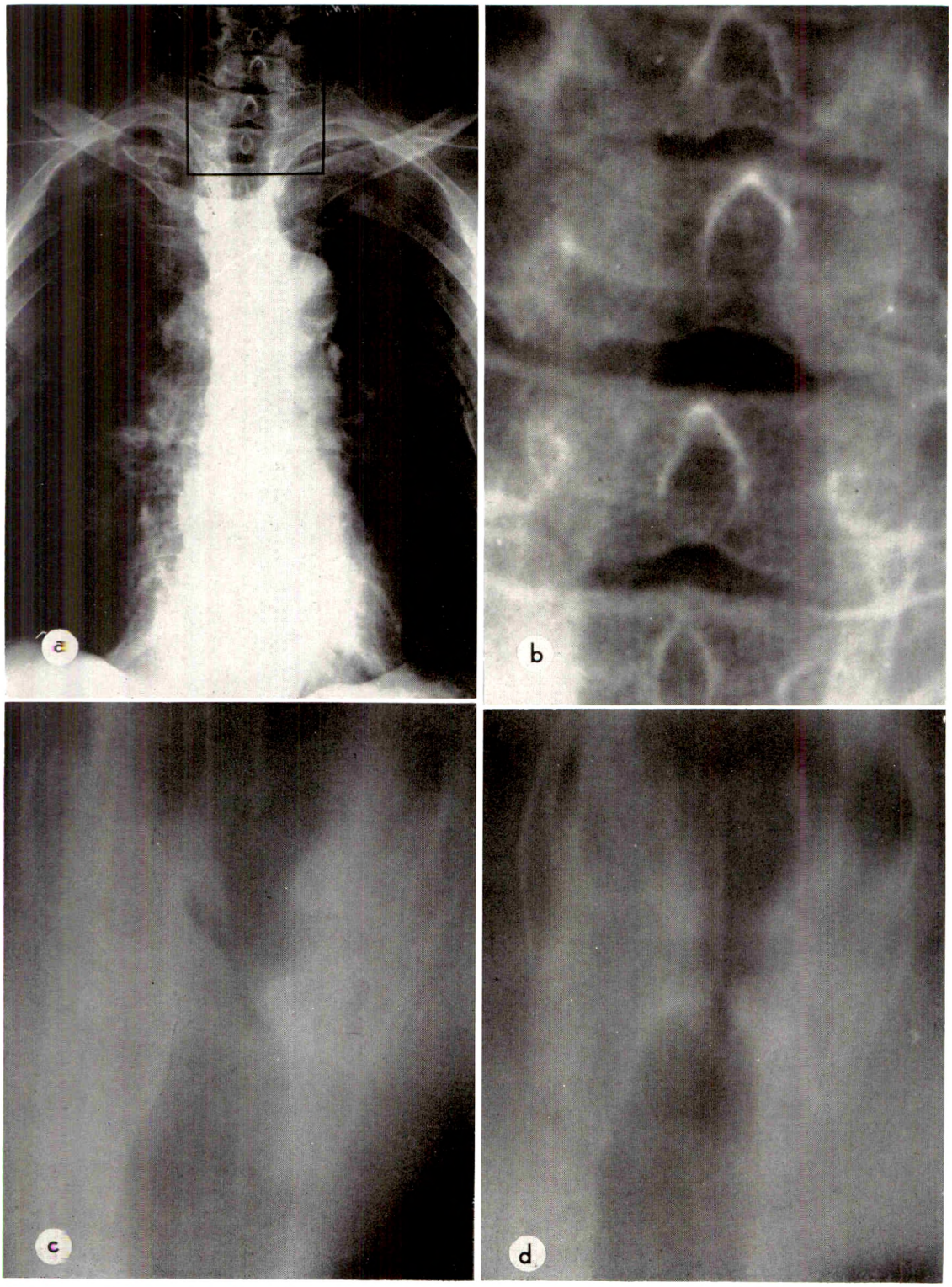


Fig. 6. Case v. (*a*, *b*, *c* and *d*) Paralysis of the left vocal cord secondary to recurrent laryngeal nerve involvement by bronchogenic carcinoma.

needs greater emphasis. Illustrative cases of abnormalities in the air column due to carcinoma of the larynx or paralysis of a vocal cord secondary to recurrent laryngeal nerve paralysis are presented.

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PRIMARY SEMINOMA OF THE MEDIASTINUM*

REPORT OF A CASE WITH AN UNUSUAL SITE OF METASTASIS AND REVIEW OF THE LITERATURE

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THE origin of primary germinal tumors of the mediastinum is not fully understood. Whether or not these growths are actually primary mediastinal tumors has been the subject of much controversy in the literature, as have been their origin, development, and the relationship between various sex-cell tumors. We are presenting the report of a case in which this rare tumor metastasized to an unusual site. We discuss the literature with respect to the theories that have been proposed to explain the origin of these neoplasms.

REPORT OF A CASE

A thirty-five year old white man was first examined at Cleveland Clinic in August, 1957. His chief symptoms were a sensation of pressure in the chest and shortness of breath. The patient had a "cigarette cough" for many years; it became productive with small amounts of yellow sputum in April, 1957. In March, 1957, a sore throat developed. In July, substernal pain became extremely severe. The patient lost 10 pounds in weight.

Physical examination. The tonsils were slightly infected. A left supraclavicular lymph node was palpable. Breath sounds were decreased over the left hemithorax, and percussion revealed that the mediastinum was widened superiorly. There were no other positive findings. The testes were normal.

Diagnostic procedures. The laboratory findings were essentially normal. Roentgenograms of the chest made on August 1, 1957, showed evidence of a mass in the left superior mediastinum which displaced the esophagus slightly to the right (Fig. 1). A biopsy of a left supraclavicular lymph node was performed, and the pathologic diagnosis was seminoma. On microscopic examination sections revealed a neoplasm

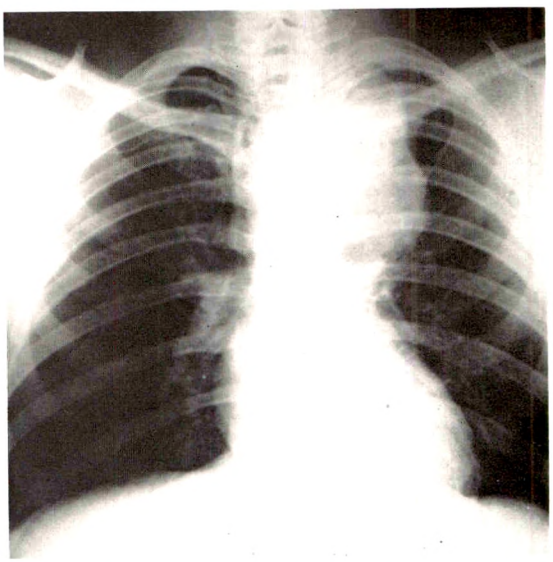


FIG. 1. Chest roentgenogram, August 1, 1957, showing a mass in the left superior mediastinum.

composed of atypical epithelial cells forming fairly uniform islands, separated from one another by slender tracts of fibrous stroma. The cells were polygonal with clear cytoplasm, and vesicular nuclei with prominent nucleoli. Scanty plasma-lymphocytic infiltration was seen throughout the sections.

Course of the disease. The patient received a tumor dose of 3,000 r to the superior mediastinum with cobalt 60 teletherapy in a period of two weeks. A roentgenogram of the chest made on September 17, 1957, showed the mediastinal mass to have markedly decreased in size (Fig. 2). The testes were re-examined and again were found to be normal. In January, 1958, the patient was asymptomatic and in excellent general condition, but in June, 1958, he experienced tightness and soreness in the throat, mainly on the right side. There was reappearance of a nonproductive cough. Ex-

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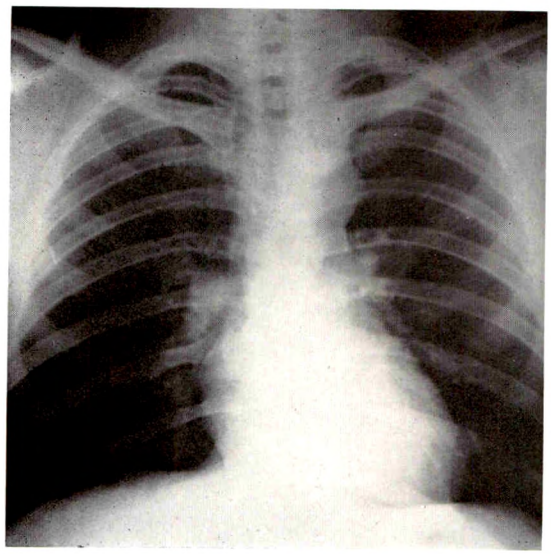


FIG. 2. Chest roentgenogram, September 17, 1957, showing marked regression of the mediastinal mass, following Co^{60} teletherapy.

amination in the therapeutic section of the Department of Radiology revealed an enlarged, ulcerated right tonsil. A biopsy was performed by a member of the Department of Otolaryngology. The pathologist's report was undifferentiated carcinoma (compatible with seminoma).

The enlargement and ulceration of the right tonsillar region regressed entirely after a tumor dose of 3,000 r with cobalt 60 teletherapy given over a period of two weeks. At the end of August, 1958, a roentgenogram of the chest showed evidence of an infiltrate in the left upper lobe, as well as increased density to the right side of the aortic arch and in the right middle lobe. The patient received another course of cobalt 60 teletherapy to the right hilus and mediastinum. A tumor dose of 3,180 r was given over a period of two weeks.

On December 19, 1958, the patient was readmitted in acute distress, with severe weakness, chest and shoulder pains, and marked shortness of breath. A tumor nodule, 2 cm. by 2 cm. in size, was present in the right tonsillar area. A roentgenogram of the chest on December 29, 1958, showed evidence of progressive and marked widening of the mediastinum with large tumor masses extending both to the right and to the left (Fig. 3). In the right hemithorax there was a large pleural effusion, apparently associated with pericardial effusion. The patient died on January 1, 1959.

Necropsy findings. A necropsy (excluding the head) revealed that the testes were normal except for greatly reduced spermatogenesis. The main pathologic diagnosis was seminoma of the anterior mediastinum. Secondary neoplasm was evidenced in the lungs, hilar lymph nodes and spleen and adrenals.

REVIEW OF THE LITERATURE

It long has been known that primary teratomata of the mediastinum do occur. Ritchie,[12] as early as 1903, reported a mediastinal growth that was, ". . . histologically identical in nature with the chorionepitheliomata." Lambert and Knox,[10] in 1920, reviewed a large number of cases and reported 2 additional cases of intrathoracic chorionepithelioma. A primary chorionepithelioma of the mediastinum was observed by Krassnianskaya[9] in 1929, and primary mediastinal teratomata with chorionepitheliomatous elements were described by Arendt[1] in 1931 and by Kantrowitz[8] in 1934. Seminoma, the most common testicular tumor, has also been encountered as a primary mediastinal tumor. Wollner, Jamplis, and Kirklin,[15] in 1955, reported 3 cases of seminoma in the mediastinum. Friedman,[5] in 1951, added 3 cases of mediastinal tumors showing the histo-

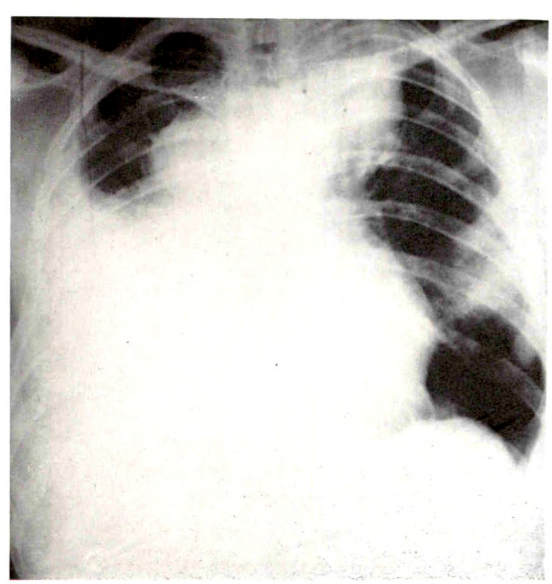


FIG. 3. Final chest roentgenogram, December 29, 1958, demonstrating bilateral mediastinal masses with pleural and pericardial effusions.

logic characteristics of germinoma. Pugsley and Carleton,[11] in 1953, found a seminomatous nodule in a primary teratocarcinoma of the mediastinum.

CLASSIFICATION

The intrathoracic germinal tumors may be classified according to cell type, as follows:

Pure: (1) teratoma, (2) chorionepithelioma, (3) seminoma.

Mixed: (1) teratoma plus chorionepithelioma, (2) teratoma plus seminoma.

THEORIES OF DEVELOPMENT

The development of germinal tumors in extragonadal sites, such as the mediastinum, the pineal gland region, the retroperitoneum, and the coccygeal area, has been the subject of interesting discussion. Most authorities believe that these tumors develop in the embryo and are present at birth. It is also rather well accepted that they are due to dissociation of tissues. According to some authors, extragonadal teratomata represent "embryonal rests," composed of entodermal and ectodermal tissues separated in the closure of the thorax.

The most practical theory, advanced by Fox and Hospers,[4] is that the primary germinal tumors of the mediastinum are due to *dissociation of totipotential cells* in the blastomere stage *before* the development of separate germ layers. These totipotential cells are thought to remain quiescent in the embryo until some future stimulus incites the cells to activity.

Another theory proposes that these tumors arise from *totipotent sex cells*. Among its advocates are Dixon and Moore,[2] Friedman and Moore,[5,6] and Scully and Parham,[13] who believe that germinoma, teratocarcinoma, chorionepithelioma, and teratoma in the pineal gland and in the region of the thymus are of germinal origin, arising from sex cells or their predecessors. How do those sex cells reach the mediastinum? Dixon and Moore[2] believe that some germ cells are left behind during the migration from the yolk sac to the gonad in early embryonic life. According to Lambert and Knox,[10] the finding of sex cells in sites outside of the gonads in some fish embryos was reported by Beard in 1902.

METASTASIS

A considerable number of the teratomata shows evidence of malignancy. It is well known that these malignant lesions may metastasize to the mediastinal lymph nodes, lungs, and sometimes to more distant sites. Only certain elements of the teratoma may take on a malignant character. Considering the developmental relationship of the germinal tumors to each other, it is not surprising that metastatic lesions of teratomata may show the histologic pattern of one of the other sex-cell tumors. According to Friedman,[5] seminomatous tissue occurs in metastatic lesions only if the primary tumor is a seminoma or if it contains seminomatous elements. Metastasis in 2 patients with chorionepithelioma of the mediastinum has been reported by Lambert and Knox.[10] Gerhartz[7] emphasized that the testicular seminoma is likely to metastasize widely to distant locations via the blood stream. Primary seminoma of the mediastinum shows a similar tendency.

With regard to the metastases of the seminoma found in our case, it is interesting that Wilson and Cares[14] reported a metastatic lesion of a mediastinal teratoma to the posterior triangle of the neck, and that Findlay[3] found malignant tissue in the mouth of a patient who had a malignant seminoma of the testis. Apparently, the mediastinal seminoma has the ability to metastasize to unusual sites.

SUMMARY

A case report of the rare primary seminoma of the anterior mediastinum with an unusual metastasis to the tonsil has been presented. The literature has been reviewed with special respect to the origin of the mediastinal seminoma.

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ACTINOMYCIN D AND ROENTGEN-RAY THERAPY IN THE TREATMENT OF METASTATIC WILMS' TUMOR*

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ACTINOMYCIN D, an antibiotic which was isolated from cultures of *Streptomyces parvallus*, has been shown to have an antineoplastic activity in tumors in children, particularly Wilms' tumor, neuroblastomas, and embryonal rhabdomyosarcomas.[2] Shaw *et al.*[3] reported definite antitumor response in 3 of 5 patients with Wilms' tumor. The method of action of actinomycin D may be by inhibiting ribonucleic acid synthesis.

The complications of actinomycin D therapy have been enumerated by Tan *et al.*[4] and consist of:

1. Redness and ulceration of the buccal mucosa beginning one to three days after an intravenous dose and lasting three to five days.

2. Vomiting four to five hours after each injection, and nausea, anorexia, occasional abdominal pain or diarrhea during therapy.

3. Erythema and occasional vesiculation and exfoliation over previously treated areas.

4. The falling out of hair and sometimes of the eyebrows in varying severity at seven to ten days after the intravenous course, with regrowth occurring after two to four weeks.

5. Leukopenia, usually temporary, occurring in the range of 2,000 white blood cells per cubic millimeter, and occasionally less than 1,000 white blood cells per cubic millimeter. This is more severe if the patient is receiving both roentgen-ray and actinomycin D therapy.

6. Platelets dropping to less than 100,000 per cubic millimeter in 30 per cent of patients.

7. Rising of the uric acid concentration in serum (14 of 93 patients in the series of Tan *et al.*[4]).

When actinomycin D and radiation therapy were given concomitantly, D'Angio *et al.*[1] noted (1) early erythema in the area of irradiation, (2) reduction in the time required for the normal progression of radiation effects, and (3) enhanced skin manifestations leading to dangerously severe local reactions following high concomitant dosages.

These effects have all been confirmed in animal experimentation.

Tan *et al.*[4] reported a favorable response in 6 of 16 patients with metastatic Wilms' tumor in whom actinomycin D therapy was used alone, and in 13 of 17 patients in whom combined roentgen-ray and actinomycin D therapy was employed.

Our discussion is limited to a brief description of a group of patients with Wilms' tumor with metastatic disease and the response of these cases to combined therapy. The dosage of actinomycin D was 75 μg./kg. body weight divided into 5 equal daily doses unless otherwise stated.

REPORT OF CASES

CASE 1. A. V., a five year old white male child, was admitted to Variety Children's Hospital on July 10, 1957 with hematuria and a left flank mass. He was transferred to Jackson Memorial Hospital, where a left nephrectomy was performed seven days later.

He received postoperative roentgen-ray therapy consisting of 3,000 r (factors 250 kv., 50 cm. target skin distance, half value layer 2.5 mm. Cu) each to left upper quadrant anterior and posterior portals. The child reportedly did

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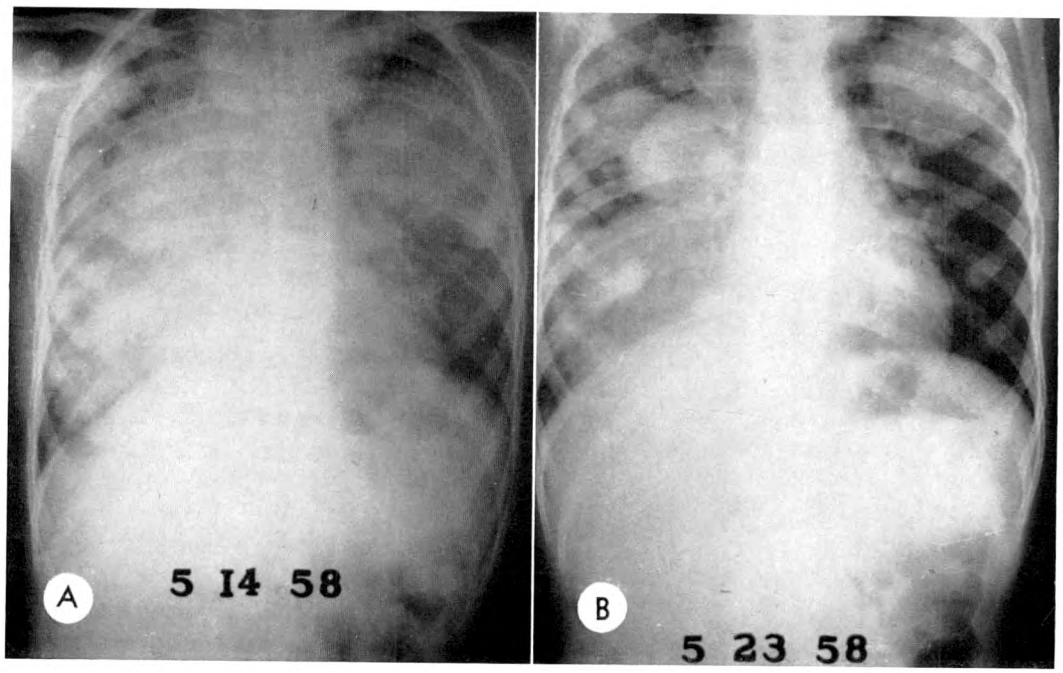


Fig. 1. Case 1. (*A*) Admission chest roentgenogram revealing far advanced metastatic disease to the lungs. (*B*) Posteroanterior chest roentgenogram five days after institution of actinomycin D therapy.

well until just prior to re-admission to Variety Children's Hospital with meningeal symptoms and marked shortness of breath ten months after the original admission. The chest roentgenogram revealed far advanced metastatic lesions in both lung fields. The child was failing rapidly, and therapy with actinomycin D was begun four days after admission (Fig. 1–4). Within eleven days marked improvement was observed. The only toxicity was vomiting, reduction in platelets from 200,000 to 21,000, and bronzing of the previous roentgen-ray portal. He was discharged from the hospital and followed in the tumor clinic.

Improvement continued for three months, at which time recurring metastases were noted in the chest. These nodules doubled in size in fourteen days, and a second course of actinomycin D was given. A five week remission was obtained. A third dose of actinomycin D was then administered, but to no avail.

Following this, roentgen-ray therapy to the chest and administration of nitrogen mustard resulted in a four week remission, and then, in an attempt to stop the progression of the lesions, mitomycin C (200 μg./kg.) was given for a period of two days. Temporary relief was afforded, but on March 2, 1959, twenty months after the original admission, the child was re-admitted and had a progressive downhill course to death. He survived ten months after what appeared to be his terminal admission and was quite comfortable and happy for about eight of these ten months.

Case II. S. L., a three year old white male child, was admitted to Variety Children's Hospital on March 17, 1958, two weeks after his mother discovered a nontender hen's egg sized mass in the left upper quadrant. Three days prior to admission the mother noted a large, swollen, not tender, bluish discoloration of the left side of the scrotum. Roentgen examination revealed a mass lesion in the superior pole of the left kidney, which displaced the kidney inferiorly, and metastases to the lungs (Fig. 5–9). At surgery all of the lymph nodes were not removed.

He received postoperative roentgen-ray therapy of 2,000 r to opposing 18×10 cm. portals, and a single concomitant course of actinomycin D. The lung lesions began to regress within two weeks and continued to regress for two months. At this time small nodular lesions were noted in the right lung, and a second course of actinomycin D, this time 90 μg./kg. in five divided

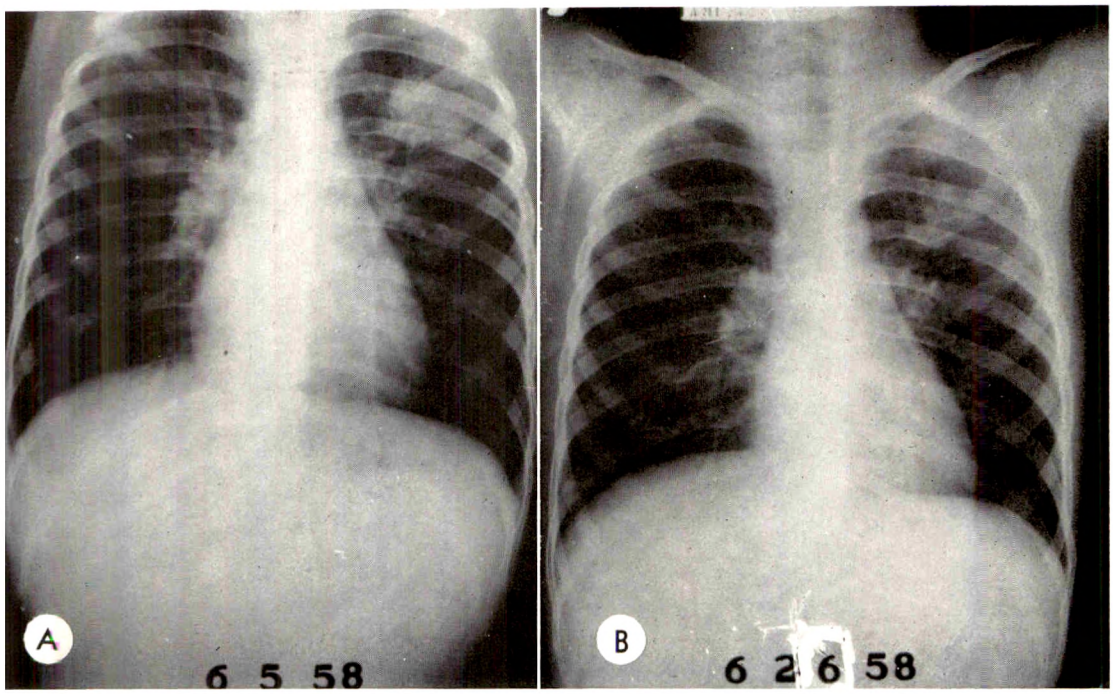


FIG. 2. Case 1. (*A*) Roentgenogram eighteen days following institution of actinomycin D. (*B*) Roentgenogram thirty-nine days after actinomycin D therapy.

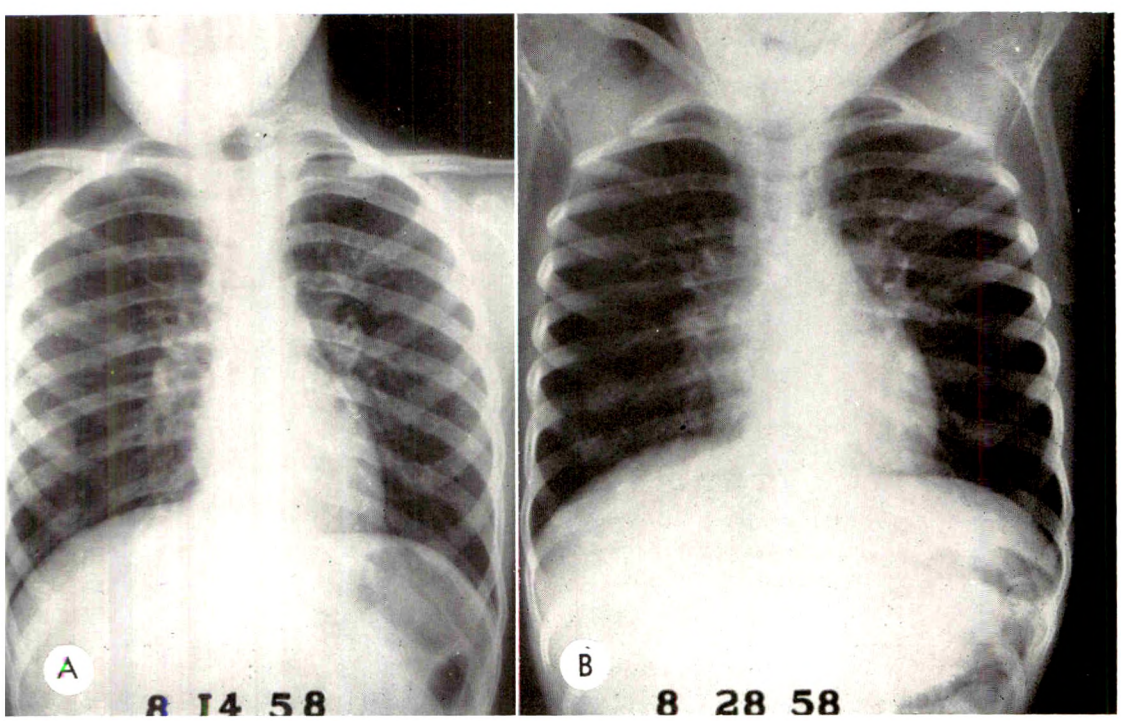


FIG. 3. Case 1. (*A*) Roentgenogram showing recurring nodule three months after institution of therapy. (*B*) Roentgenogram showing some regression two weeks after second course of actinomycin D therapy.

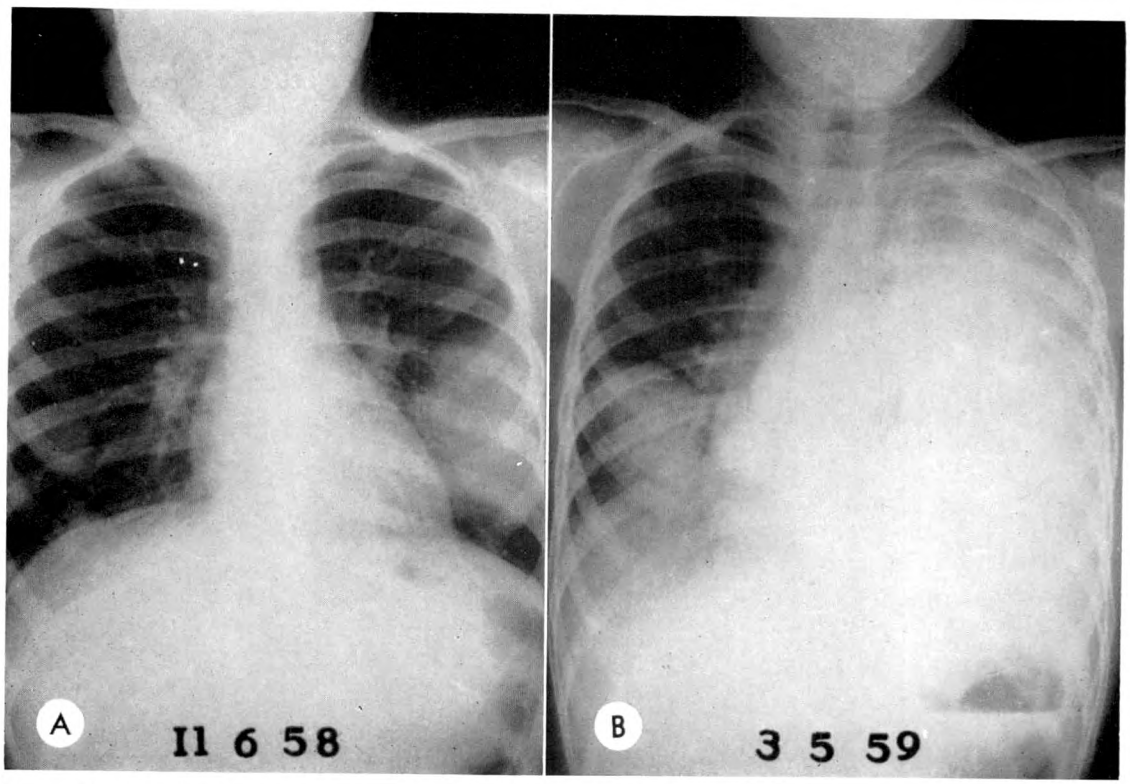


Fig. 4. Case I. (*A*) Roentgenogram showing recurrent metastatic nodules six months after start of actinomycin D therapy. (*B*) Chest roentgenogram on final admission.

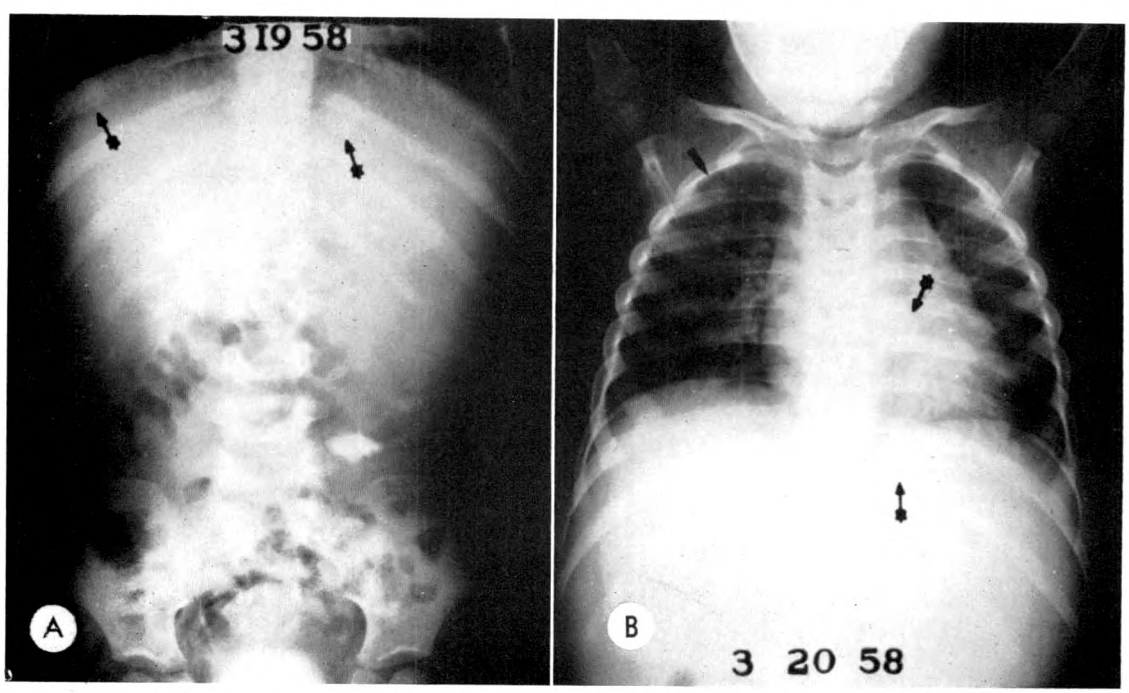


Fig. 5. Case II. (*A*) Intravenous pyelogram showing mass lesion displacing left kidney inferiorly, and two metastatic lesions in the lungs (arrows). (*B*) Admission chest roentgenogram revealing bilateral metastatic Wilms' tumor.

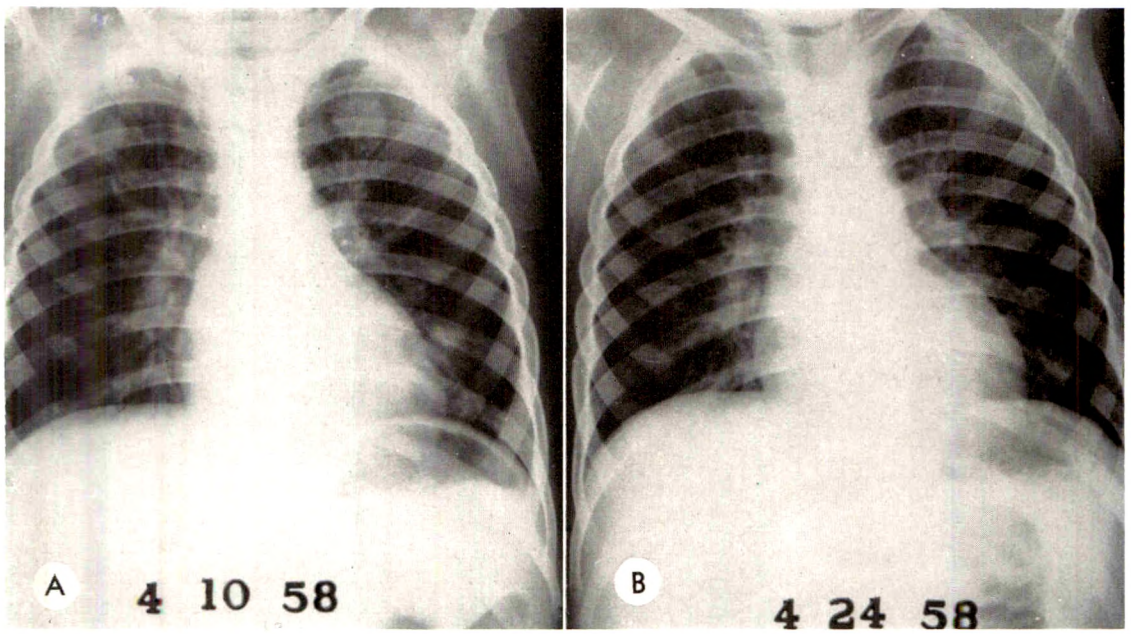


Fig. 6. Case II. (*A*) Chest roentgenogram showing metastatic lesions at beginning of combined therapy. (*B*) Roentgenogram two weeks later showing regression of metastatic lesions.

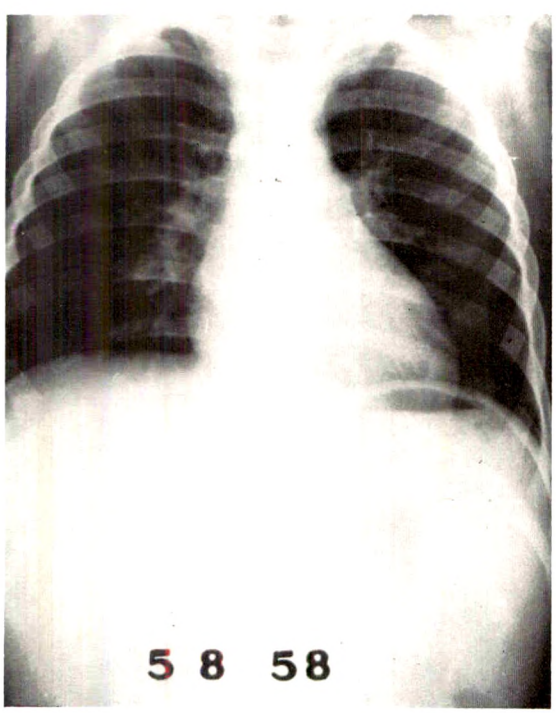


Fig. 7. Case II. Roentgenogram at completion of therapy.

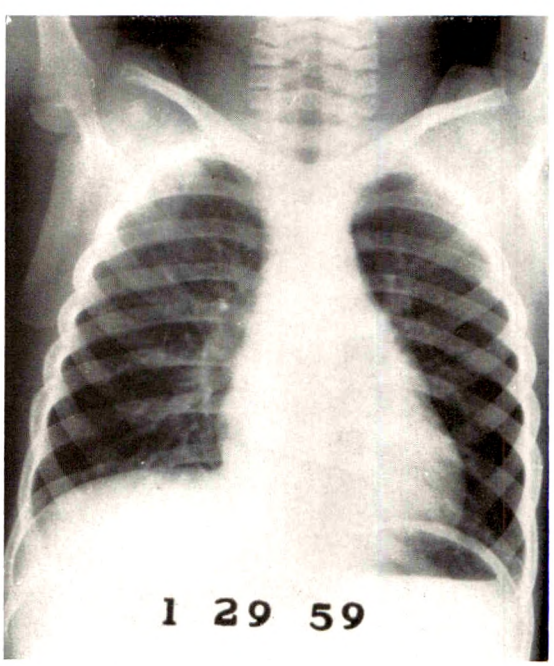


Fig. 8. Case II. Roentgenogram eight months after treatment.

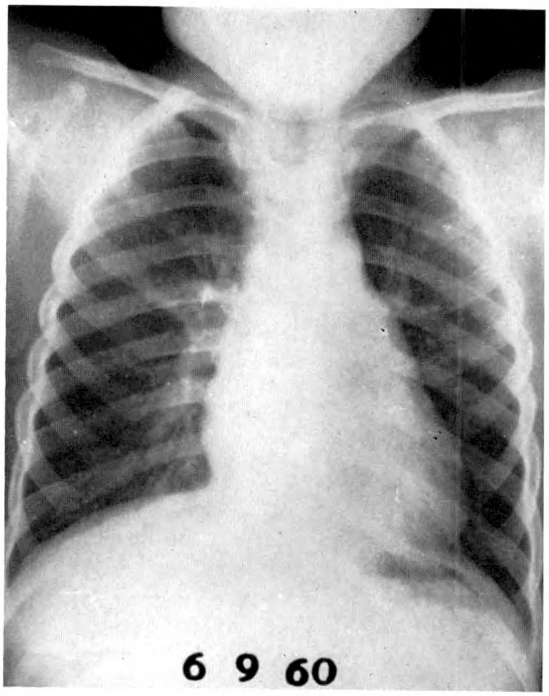


Fig. 9. Case II. Negative chest roentgenogram two years following treatment.

daily doses, was administered. Marked erythema was noted in the previously irradiated areas. The metastases disappeared within four weeks, and the child has remained well to date, three years after his initial admission.

Case III. G. V., a thirteen year old white male child, was admitted to Jackson Memorial Hospital on November 28, 1958, seven years after the removal of a retroperitoneal ganglioneuroma. At that time he was given roentgen-ray therapy through two opposing left abdominal ports, a 2,000 r air dose being administered to each port. Following this no recurrence was noted.

On this admission he complained of right lower quadrant pain. At surgery a large hemorrhagic right kidney tumor which extended into the renal vein was discovered. The pathologic diagnosis was Wilms' tumor with involvement of the renal vein. The patient received post-operative roentgen-ray therapy consisting of a 2,400 r air dose to a 10×12 cm. right anterior port and a 2,600 r air dose to a right posterior upper abdominal 10×12 cm. portal (factors 250 kv., 50 cm. target skin distance, half value layer 2.5 mm. Cu). Roentgenograms revealed no metastases to bones, skull or chest.

Two months later metastatic lesions (Fig. 10) to the chest were observed, and actinomycin D was administered. A five week remission was obtained, after which progression of metastases was again noted and a second course of actinomycin D was started. The patient's disease, however, had only a two week remission and although a third course of actinomycin D was begun, he expired.

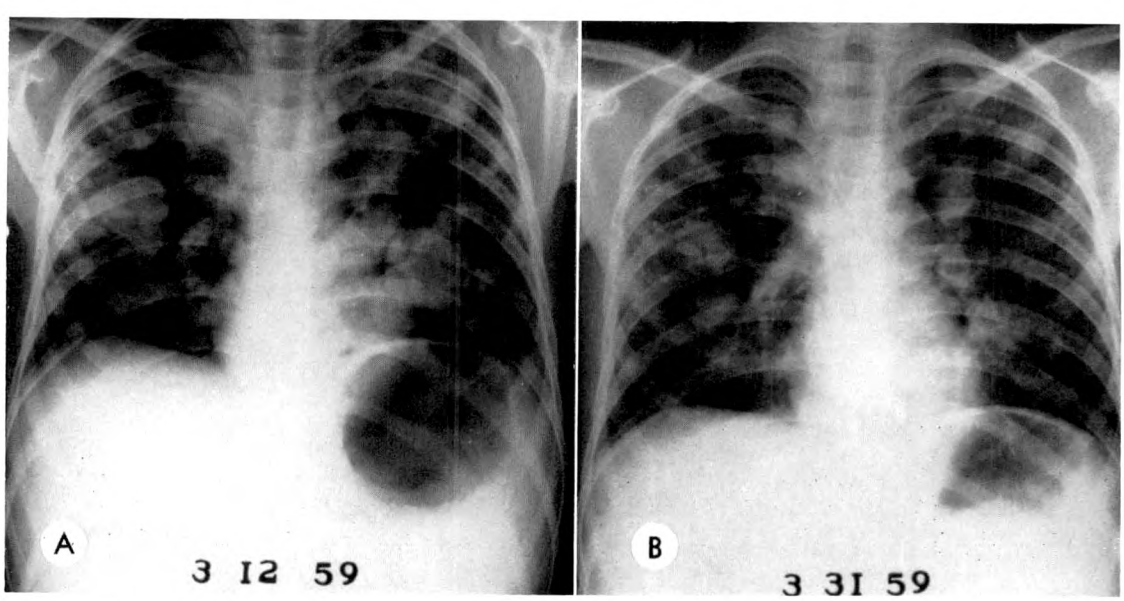


Fig. 10. Case III. (*A*) Roentgenogram showing far-advanced metastatic Wilms' tumor to the lung fields. (*B*) Roentgenogram nineteen days after institution of actinomycin D therapy.

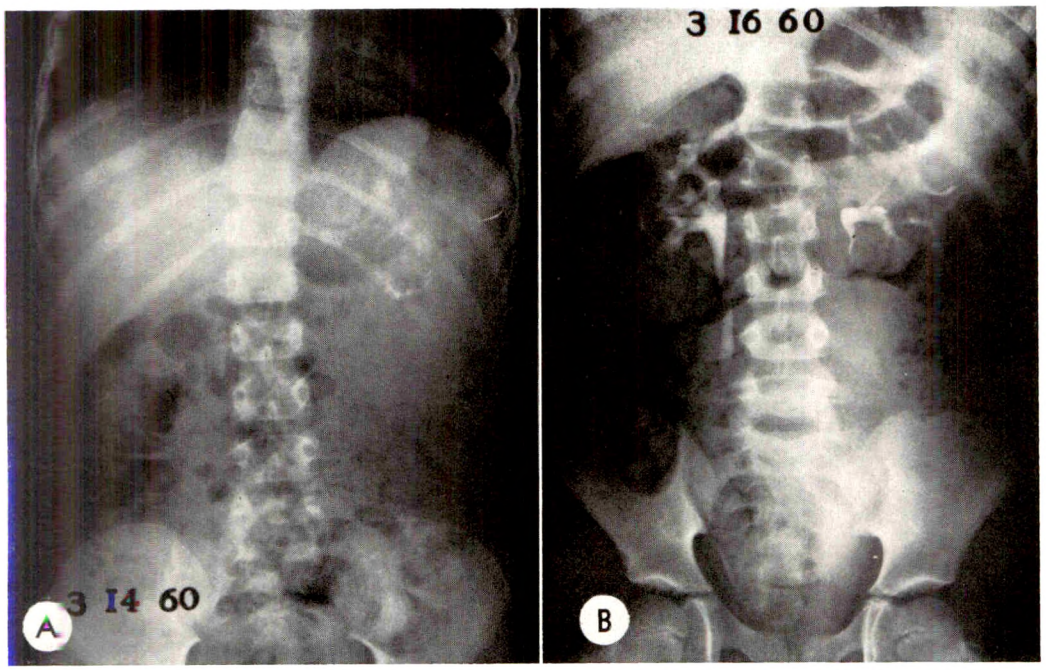


FIG. 11. Case v. (*A*) Admission abdominal roentgenogram revealing calcified mass in the left renal area. (*B*) Intravenous pyelogram revealing mass lesion (Wilms' tumor) in the upper pole of the left kidney.

CASE IV. F. S., a sixteen month old Negro female child, was seen at Variety Children's Hospital on December 28, 1958 with a history of abdominal swelling of two weeks' duration. The abdomen was markedly distended with prominent veins. A large right-sided abdominal mass was palpated, the lower border of which was just above the iliac crest. Admission roentgenograms disclosed a negative chest. An intravenous pyelogram demonstrated a large mass lesion displacing the right kidney and ureter. A bone survey was negative.

Surgical exploration revealed a large Wilms' tumor of the right kidney. Silver clips were placed at the limits of the tumor bed for roentgen-ray beam direction. The pathologic diagnosis was Wilms' tumor, with metastases to the posterior and anterior lymph nodes.

Postoperative roentgen-ray therapy consisted of two 8×14 cm. opposing portals (factors 220 kv., 50 cm. target skin distance, half value layer 2.0 mm. Cu, tumor dose 4,380 r) with concomitant actinomycin D. Toxicity was noted by vomiting and diarrhea. The radiation reaction was very severe. The postirradiation roentgenogram of the chest was negative. Examination two years after surgery revealed normal growth and development without evidence of metastases.

CASE V. S. P., a seven year old white female child, was admitted to Variety Children's Hospital on March 11, 1960 with a chief complaint of severe pain in the lower back and rigidity in the back and neck.

Preliminary roentgenograms of the thoracolumbar spine (Fig. 11–13), revealed a calcified mass in the left upper quadrant. An intravenous pyelogram demonstrated distortion of the upper calyceal system of the left kidney and displacement of the kidney inferiorly. A left nephrectomy was performed. The pathologic diagnosis was Wilms' tumor of the left kidney without evidence of metastases to the regional lymph nodes or renal vein.

The patient received nitrogen mustard and roentgen-ray therapy (factors 220 kv., 50 cm. target skin distance, half value layer 2.0 mm. Cu, tumor dose 4,350 r, 10×15 cm. opposing portals) which was started on the first postoperative day.

Metastases to the lung were discovered three and one-half months after admission. Actinomycin P_2 was given for five daily doses. The patient developed nausea, vomiting, and a drop in the platelet count from 190,000 to 36,000. The lung lesions showed no change for a period of one month, and then progression was seen. A course of actinomycin D was then given.

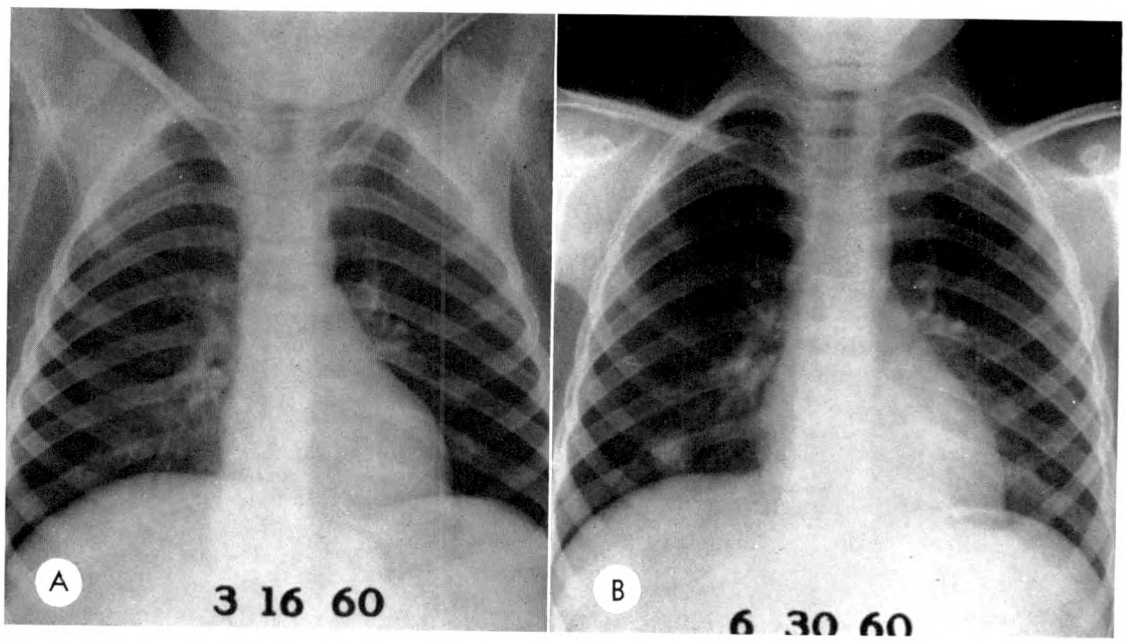


FIG. 12. Case v. (*A*) Negative chest roentgenogram on admission. (*B*) Roentgenogram showing metastatic Wilms' tumor of the right lower lobe, three months after surgery and postoperative irradiation.

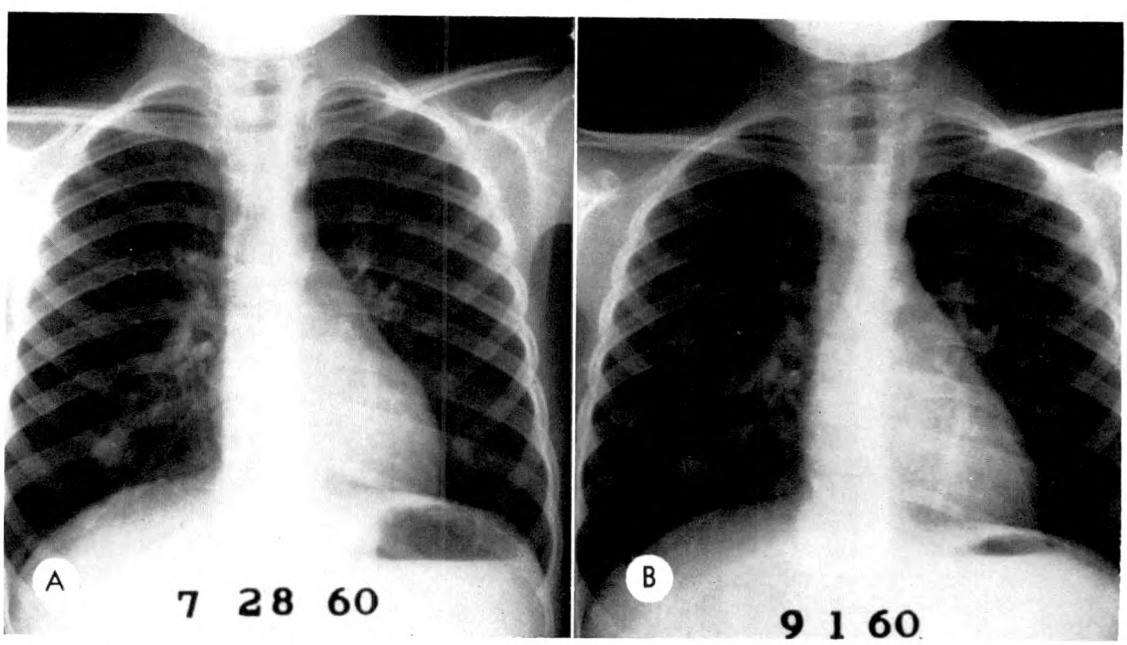


FIG. 13. Case v. (*A*) Roentgenogram showing no change of lesion one month following institution of actinomycin P_2 therapy. (*B*) Roentgenogram showing status of lesion two months following institution of therapy.

SUMMARY

Actinomycin D has a definite antineoplastic effect on metastases of Wilms' tumor. The toxic effects of the drug in the dosage used were not severe. There appears to be a potentiation of effect when actinomycin D and roentgen-ray therapy are used concomitantly. Of the 5 cases presented, the best results were obtained by the initial concomitant use of actinomycin D and roentgen-ray therapy. Two of the 5 patients in whom concomitant therapy was used initially and in whom metastases were present are well to date, 1 for three years and 1 for two. One patient in whom metastases were not found initially and who received postoperative irradiation and nitrogen mustard developed metastases within three months. This has been helped by actinomycin P_2 therapy. The other 2 patients were treated for metastatic disease primarily with actinomycin D and received moderate palliation.

CONCLUSION

Five cases of metastatic Wilms' tumor are presented, and their varying response to actinomycin D and roentgen-ray therapy is discussed.

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THE ROENTGEN FINDINGS IN LYMPHOSARCOMA OF THE SMALL INTESTINE*

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THE roentgen alterations produced by lymphosarcoma of the small intestine have been considered, in general, to be too varied and nonspecific to permit a definite diagnosis. With increasing experience with small intestinal lymphosarcoma and with the recognition of the abnormal patterns produced by other small intestinal ailments, it has become apparent that primary lymphosarcoma of the small intestine often presents an appearance which is highly suggestive of the underlying pathologic alterations. It is true that lymphosarcoma of the small intestine may present in a variety of forms which, at first glance, may seem to bear little relation to each other. It will be seen, however, that the differences in the changes produced are primarily a function of the direction of growth and the multiplicity of the lesions.

Early recognition of primary neoplasms of the small intestine is difficult due to the paucity of localizing symptoms and signs relating to the disease until it is far advanced. This is particularly true of primary lymphosarcoma of the small intestine because obstruction is infrequent, in contrast to carcinomas in this region, where obstruction is often the first presenting sign. The most useful diagnostic aid is roentgen study.

A classification of the roentgen changes, therefore, is of practical usefulness. The purpose of this paper is to present the roentgen findings in a series of 75 proved cases of primary lymphosarcoma of the small intestine. They may be classified as follows: (1) multiple small nodular form; (2) infiltrating form; (3) polypoid form (intussusception); (4) endo-exoenteric form with extensive excavation, perforation and fistula formation; and (5) predominantly invasive form of the mesentery with (a) large extraluminal masses (single or multiple, with extrinsic pressure upon the small intestine), and (b) production of the sprue pattern.

GENERAL CONSIDERATIONS

The frequency of lymphosarcoma in the various portions of the small intestine roughly parallels the distribution of lymphoid tissue within the small bowel. Accordingly, it is most commonly found in the ileum where larger lymphoid collections (Peyer's patches) exist.

The tumor may arise in the lymphoid tissue of the mucosa or submucosa. It has a tendency to extend along the long axis of the bowel and may take origin from multiple sites. This is in contrast to the usual behavior of carcinomas in this region which produce a single short segmental constricting lesion.

In the initial stages, lymphosarcoma may appear as a discrete, thickened, nonulcerated plaque with relatively intact overlying mucosa. Presumably, if it arises superficially, that is, in the mucosa, growth may be predominantly towards the lumen causing no remarkable rigidity in the adjacent bowel wall. As a result, exaggerated peristalsis, occasioned by the intraluminal mass, in an attempt to expell the mass may produce an intussusception with subsequent intestinal obstruction.

Lymphosarcoma, however, may extend intramurally causing a diffuse thickening of the wall of the small intestine over a considerable distance. When this occurs in the submucosa, the folds of the mucosa may appear intact. Sometimes they may be

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smoothed out by the submucosal thickening and, on occasion, may even appear coarsely thickened. When the infiltration is more superficially located, the overlying mucosa may be thrown up into innumerable small polypoid projections. This diffusely infiltrating form is not associated with any single mass but occurs along the course of the involved bowel; alternating areas of greater and lesser involvement may be found producing a grossly irregular, rigid, unchanging appearance.

In contrast to this type of extension, that is, along the longitudinal axis of the bowel, growth may occur essentially outwards. In this situation, the mass is usually large and both endo- and exointestinal in position. As the mass grows, it destroys the intestinal wall and extends into the mesentery, infiltrating and destroying adjacent intestinal loops. Ulceration of the tumor occurs with the formation of many intercommunicating channels within the tumor mass as well as into the adjoining involved bowel loops. Ulceration and necrosis within the tumor continue producing a large irregular excavation which communicates with several loops of bowel. Perforations that occur, therefore, are rarely into the free peritoneal cavity but rather into the agglutinated mass of tumor, mesentery and small intestine.

Lymphosarcoma is a medullary tumor and as such does not evoke a desmoplastic response. As a result, there is little tendency for scirrhous tissue to form and stenosis to occur. A certain degree of narrowing of the bowel lumen may be observed due to extrinsic compression and marked thickening of the bowel wall, but stricture formation of sufficient severity to cause intestinal obstruction is rare. When it occurs, it is associated with ulceration and secondary infection. In one instance in the present series the ulceration which had evoked mechanical intestinal obstruction by producing marked spasm was not located in the tumor itself but immediately adjacent to it (Fig. 9*B*). This situation is extremely rare. Intestinal obstruction in lymphosarcoma is most often incident to intussusception.

In some cases, the infiltrated bowel wall reveals a remarkable local segmental dilatation, sometimes of "aneurysmal" character. The apparent atonicity has been explained as the result of destruction of the muscular coat by the tumor as well as involvement of the nerve plexuses.

Diffuse involvement of the mesentery by extraluminal extension of lymphosarcoma may produce alterations in absorption of nutrients from the intestinal tract. Fats, being the most difficult substances to absorb, are generally the first to be affected and steatorrhea may result. The clinical and laboratory findings may then be indistinguishable from those seen in idiopathic sprue. However, failure to respond to the usual therapy for idiopathic sprue or the subsequent development of other evidence of lymphosarcoma leads eventually to the correct diagnosis.

ROENTGEN FINDINGS

1. *Multiple small nodular defects* (Fig. 1, *A* and *B*). These appear roentgenographically as multiple pea-sized intraluminal nodules which alter the mucosal pattern of the bowel and produce an irregular, coarse scalloping of the bowel contour. The bowel lumen may be of normal or increased caliber. It is not narrowed. These changes are usually found in the ileum and involve segments varying from one to two feet in length. The involved segment retains its pliability and is not fixed in position.

This form may occur as the sole manifestation of the disease or may be associated with other small intestinal changes. We have observed 5 such cases. In 3, the colon was also involved. The colonic changes are similarly nodular and may simulate the roentgen alterations seen in familial polyposis. The changes in the colon may not be seen as easily as those in the small intestine because the lumen of the colon is large and distensible and the tiny nodular

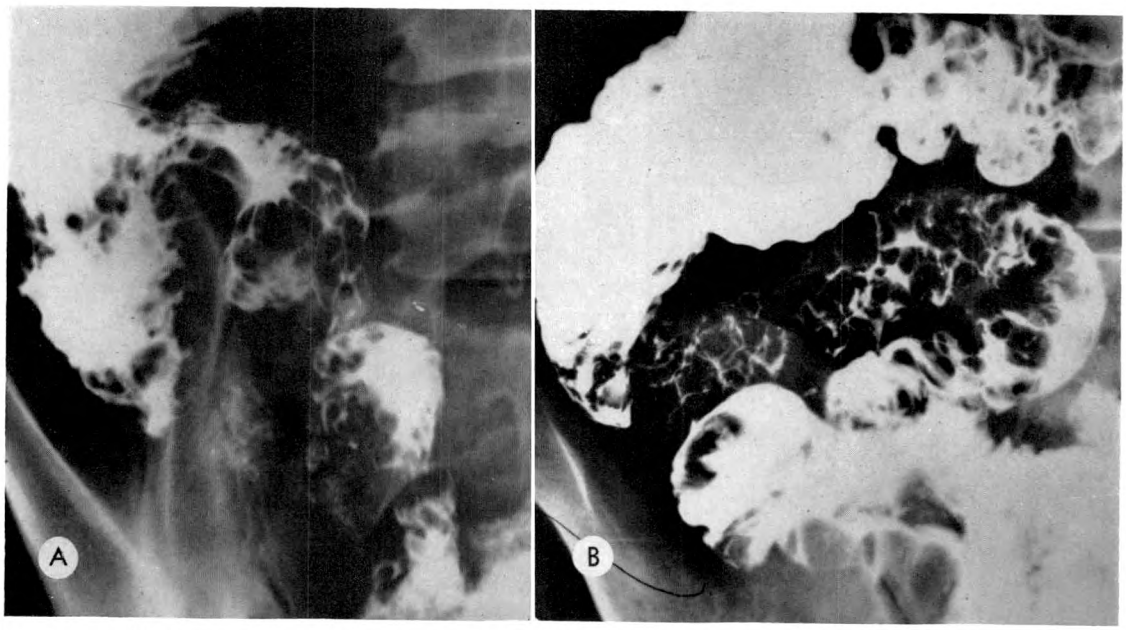


Fig. 1. (*A*) There are multiple tumor nodules of varying size in the terminal ileum, cecum and ascending colon. The terminal ileum is slightly dilated. (*B*) The mucosal pattern is replaced by numerous polypoid intramural and intraluminal defects which alter the caliber of the bowel lumen. There is no evidence of any obstruction.

defects may be obscured by the larger amounts of barium utilized in studying it. In 1 case, the stomach appeared to be involved independently of the small intestinal lesion.

2. *Infiltrating form* (Fig. 2, *A* and *B*; 3, *A* and *B*; 4, *A* and *B*; and 5, *A* and *B*). The bowel wall may become diffusely infiltrated by lymphosarcoma and thickened for considerable lengths. The degree of thickening may vary from area to area, producing irregular segments of narrowing and relative dilatation. The degree of narrowing is never as marked as that observed in carcinoma or inflammations. The mucosal folds may be flattened and effaced, or they may be thickened and thrown up into irregular nodular projections producing coarse, irregular scalloping of the bowel contour with intraluminal filling defects of varying sizes. The mural thickening causes separation and straightening of the bowel loops which stand out clearly from the closely approximated, normal small intestinal loops. The barium column may have a mottled appearance due to increased secretions from within the lumen of the affected segment.

The infiltration may be limited to short segments, either single or multiple, which appear as short areas of eccentric narrowing of the bowel lumen with effacement or thickening of the mucosal folds and evidence of tumor formation. Marked rigidity of the involved segment is not seen nor is there sufficient stenosis to produce dilatation of the small intestine proximally.

Associated with this segmental lesion, small nodular defects along the contour of the bowel lumen are frequently found. They may be situated at some distance from the more conspicuous lesion. They may be single or multiple and are generally less than 1 cm. in diameter. They may widen the normal interval between valvulae but do not extend across the full width of the bowel lumen.

Another form of segmental infiltration of the bowel wall in lymphosarcoma is that which extends for fairly short distances and is accompanied by marked localized dilatation. This has been termed aneurysmal dilatation. The increased thickness of the

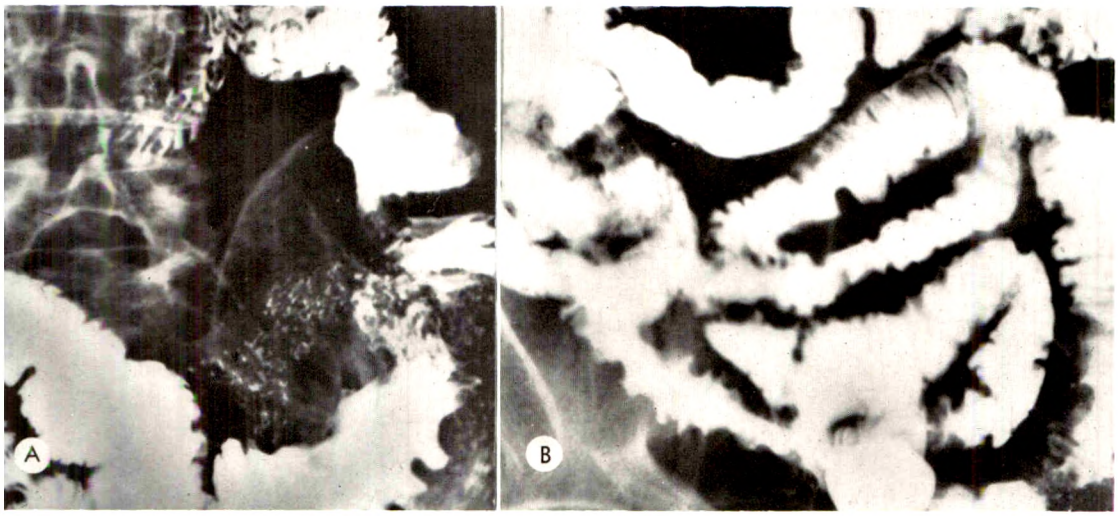


FIG. 2. (*A*) Infiltration of multiple short segments of the jejunum by lymphosarcoma. In this case, two areas are involved. The proximal area of involvement shows a segmental area of irregular dilatation of the bowel lumen, destroyed mucosal folds and a suggestion of an intramural mass. The second lesion, a few inches caudad, shows flattening and rigidity of one wall and abnormal valvular markings on the contour of the opposite wall. (*B*) There is thickening and blunting of the folds with some encroachment upon the bowel lumen but no obstruction. In some areas, small tumor nodules can be identified along the contour of the bowel lumen.

bowel wall is demonstrated by increased separation from adjacent loops. The barium tends to pool within the widened lumen and no mucosal pattern can be seen. The contours of the dilated segment may be smooth, coarsely irregular or show scalloping and nodularity due to intramural tumor formation. The adjacent mucosa may appear intact or thickened and nodular.

3. *Polypoid form* (Fig. 6, *A* and *B*). When the tumor has grown to a size sufficient to produce a discrete intraluminal mass and

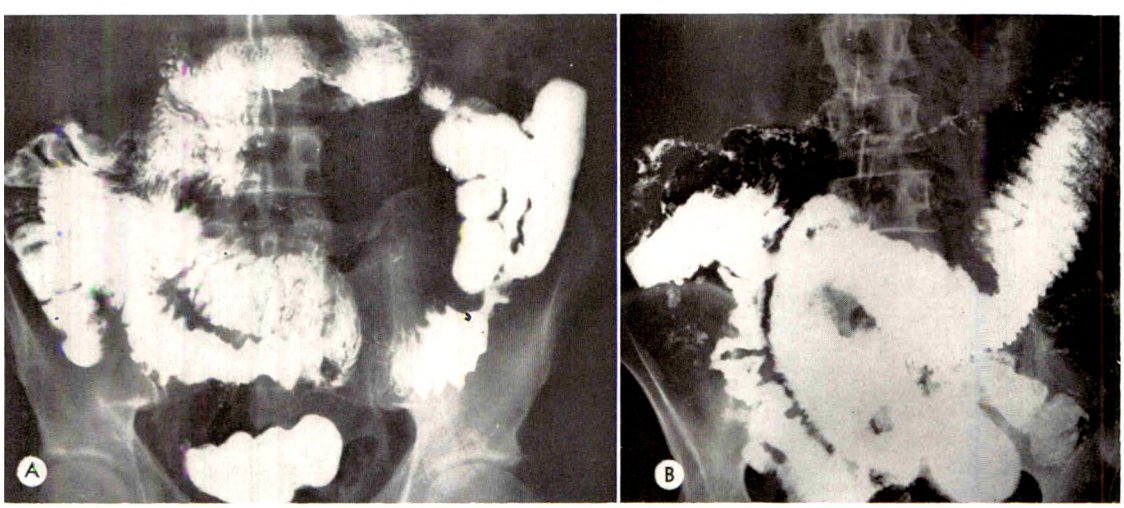


FIG. 3. (*A*) There is slight dilatation of the distal jejunum which shows thickening and blunting of the folds, with effacement in some areas. The contours are coarsely irregular. One short segment of narrowing is seen. This appearance simulates that of the nonstenotic phase of regional enteritis. (*B*) Diffuse infiltrating lymphosarcoma of the jejunum and ileum. In some segments the lumen is dilated with irregular or saw-toothed contours. Elsewhere the folds are thickened.

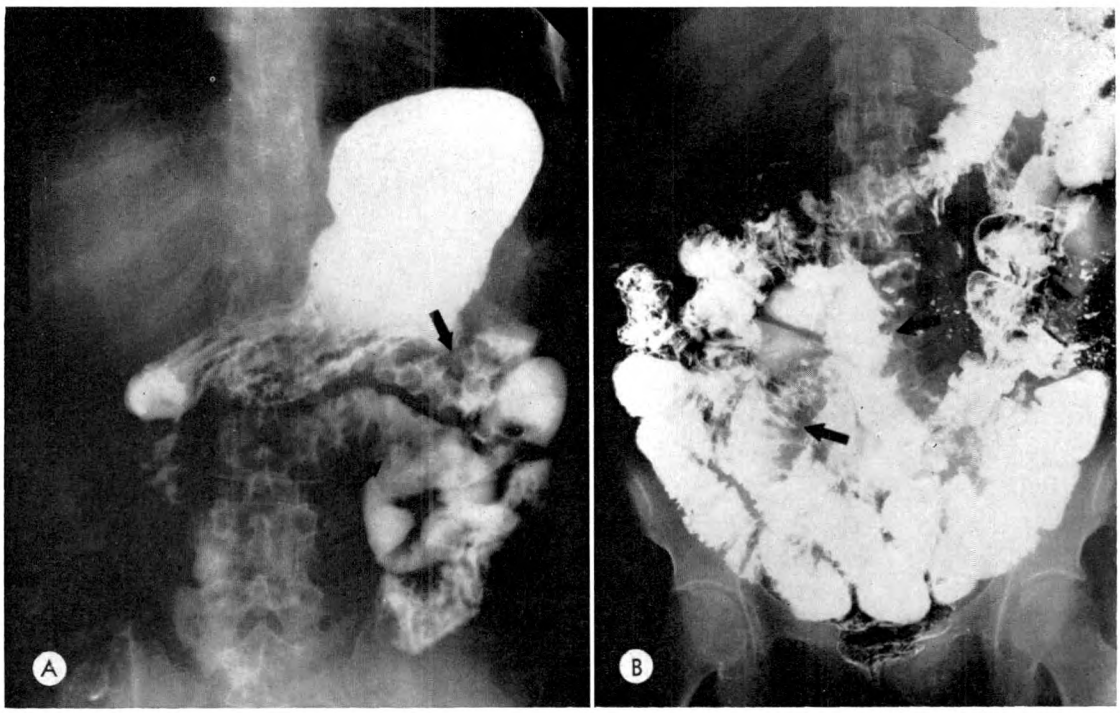


Fig. 4. (*A*) Diffuse infiltrating lymphosarcoma involving the entire small intestine. In the jejunum, multiple intramural and intraluminal tumor nodules (arrow) alter the bowel contour. (*B*) In the ileum, the bowel is dilated. The mucosal folds are thickened and blunted. Mural tumor nodules can still be identified (arrows).

is without intramural extension, it may be drawn forward by peristalsis, forming a pseudopedicle, and may become the lead-point of an intussusception. Unless there are other clues to the nature of the underlying lesion, the cause of the intussusception cannot be determined from the roentgenograms. The polypoid tumor itself is rarely visualized on roentgen study because it is prone to intussusception and may become obscured by the intussusceptum and intussuscipiens.

Four times in this series, intussusception only was seen. In 2 other instances, marked thickening of the mucosal folds in the region of the intussusception and fistulas and nodularity of the adjacent mucosa were noted. In 1 other case, there were multiple polypoid lesions with ulceration of the mucosa, numerous fistulas and dilatation of the involved bowel.

4. *Endo-exoenteric form with excavation* (Fig. 7, *A* and *B*; and 8, *A* and *B*). In this instance, a large excavated mass with multiple fistulas and communications with the adjacent small bowel is seen.

The roentgen findings are usually bizarre. The characteristic finding is an extensive irregular amorphous patch of barium which does not conform to the intestinal lumen and communicates with the surrounding small intestinal loops. The adjacent small intestinal loops are displaced by the large mass. Fistulas are not infrequent.

The earlier changes are seen less frequently. Before massive excavation occurs, the tumor and the involved portion of the small intestine may be criss-crossed by many intercommunicating channels connecting the tumor with the lumen of the small intestine. These channels appear as amorphous barium streaks of varying caliber. In 1 such case, because of the presence of the altered intestinal loops and the fistulas, the diagnosis of regional enteritis was made. Subsequent events leading to massive excavation of the involved area indicated the presence of necrotic neoplasm.

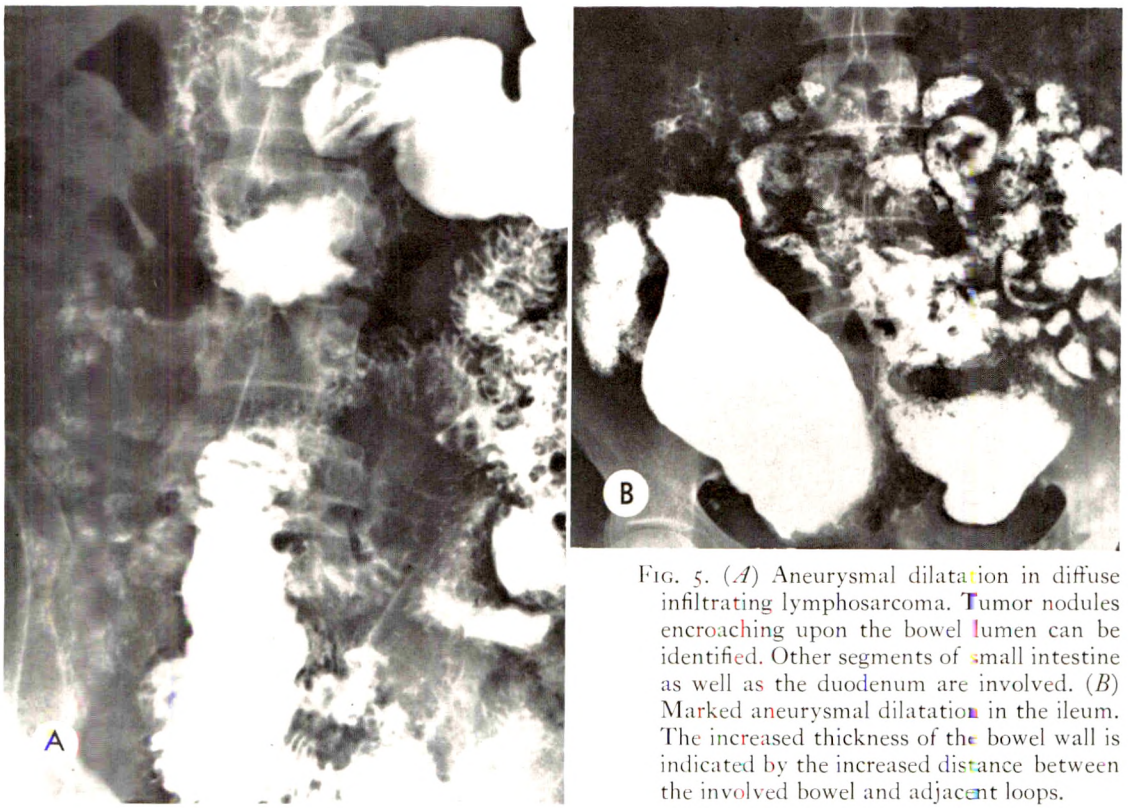


FIG. 5. (*A*) Aneurysmal dilatation in diffuse infiltrating lymphosarcoma. Tumor nodules encroaching upon the bowel lumen can be identified. Other segments of small intestine as well as the duodenum are involved. (*B*) Marked aneurysmal dilatation in the ileum. The increased thickness of the bowel wall is indicated by the increased distance between the involved bowel and adjacent loops.

This appearance is not pathognomonic of lymphosarcoma and has been observed in other sarcomatous tumors of the intestinal tract.

5. *Predominantly invasive form of the mesentery*. (a) Large extraluminal masses. The greater portion of the tumor may grow centrifugally and produce large extraluminal masses which can attain huge proportions and even extend into the retroperitoneum. They manifest themselves roentgenologically by displacement of the abdominal organs, pressure defects upon the adjacent viscera and invasion of the intestinal wall. The presence of a mass alone is not diagnostic of lymphosarcoma unless mural alterations which characterize this type of growth are seen in the small intestine.

It is again of interest to note that in this form of lymphosarcoma, intestinal obstruction is infrequent. In metastatic carcinoma, however, in which there is involvement of the mesentery and infiltration of the bowel, incomplete obstruction is not uncommon.

(b) Production of the sprue pattern (Fig. 9*A*). Along with clinical and laboratory findings of sprue, which can be produced when there is diffuse involvement of the mesentery, a roentgen picture simulating sprue also may be found in lymphosarcoma. Eight such cases have been observed in this series. In 6, the sprue pattern was seen with dilatation of the small intestinal loops, hypersecretion and segmentation of the barium column. The findings were indistinguishable from those seen in idiopathic sprue and a definite diagnosis of lymphosarcoma could not be made. In 2 additional cases, there was evidence of extraluminal masses with displacement and invasion of the small bowel loops superimposed upon the sprue pattern.

DIFFERENTIAL DIAGNOSIS

1. *Hodgkin's disease* (Fig. 10, *A* and *B*). In general, Hodgkin's disease produces the same kind of lesions in the small intestine as lymphosarcoma; however, perforation, fistulas and aneurysmal dilatation have not

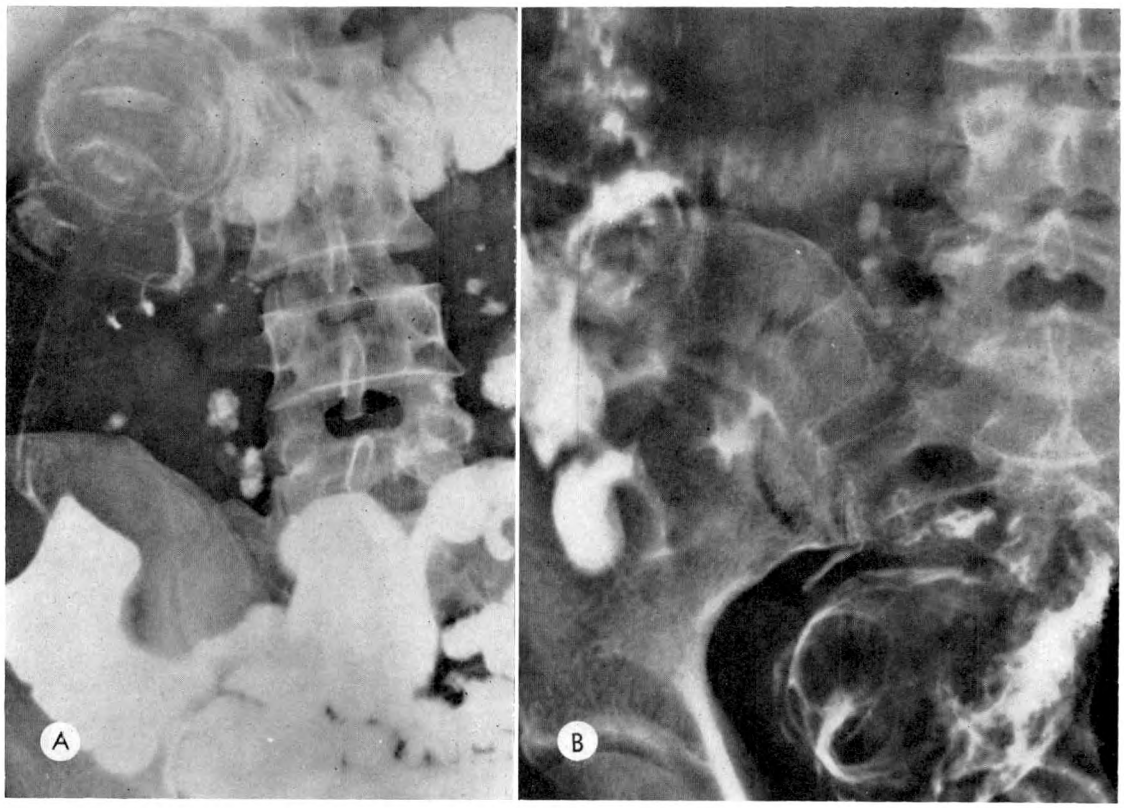


FIG. 6. (*A*) Polypoid lymphosarcoma of the terminal ileum resulting in an ileocolic intussusception with minimal obstruction. The lesion in the ileum is obscured by the intussusceptum. (*B*) Large lobulated polypoid lymphosarcoma of the terminal ileum seen after evacuation of a barium enema.

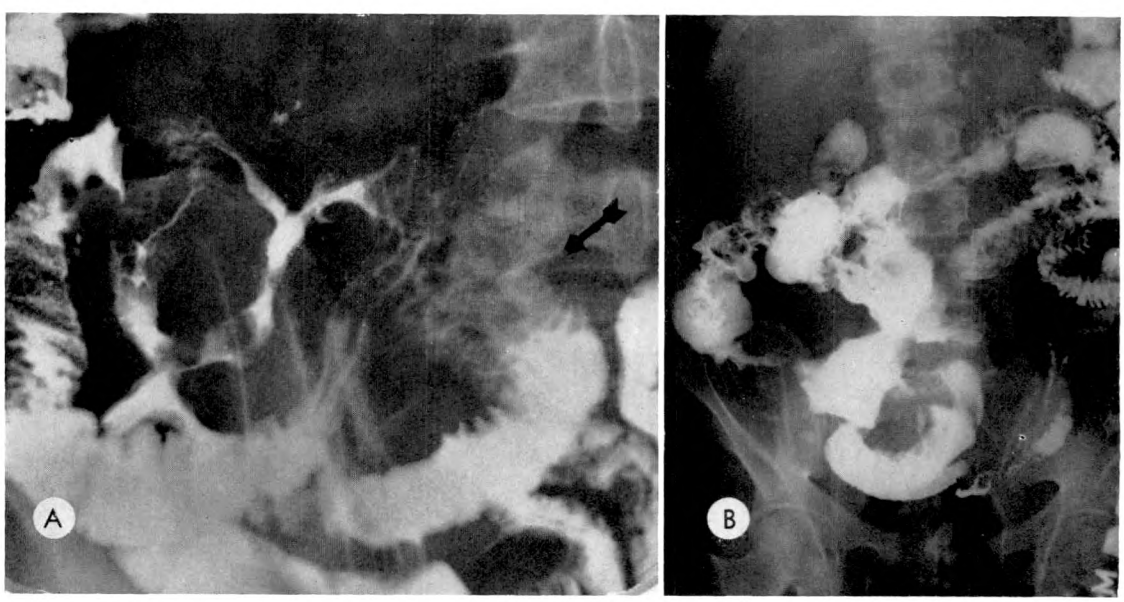


FIG. 7. (*A*) Endo-exoenteric lymphosarcoma of the distal ileum. The normal bowel lumen is replaced by many intercommunicating tortuous tracts through the tumor. The arrow points to the nodular mucosal pattern proximal to the mass. The lumen of this segment is not narrowed. (*B*) Three months later, there is a large irregular, triangular, excavated area within the tumor containing an amorphous collection of barium. The mucosal folds in the adjacent small intestinal loops are considerably thickened.

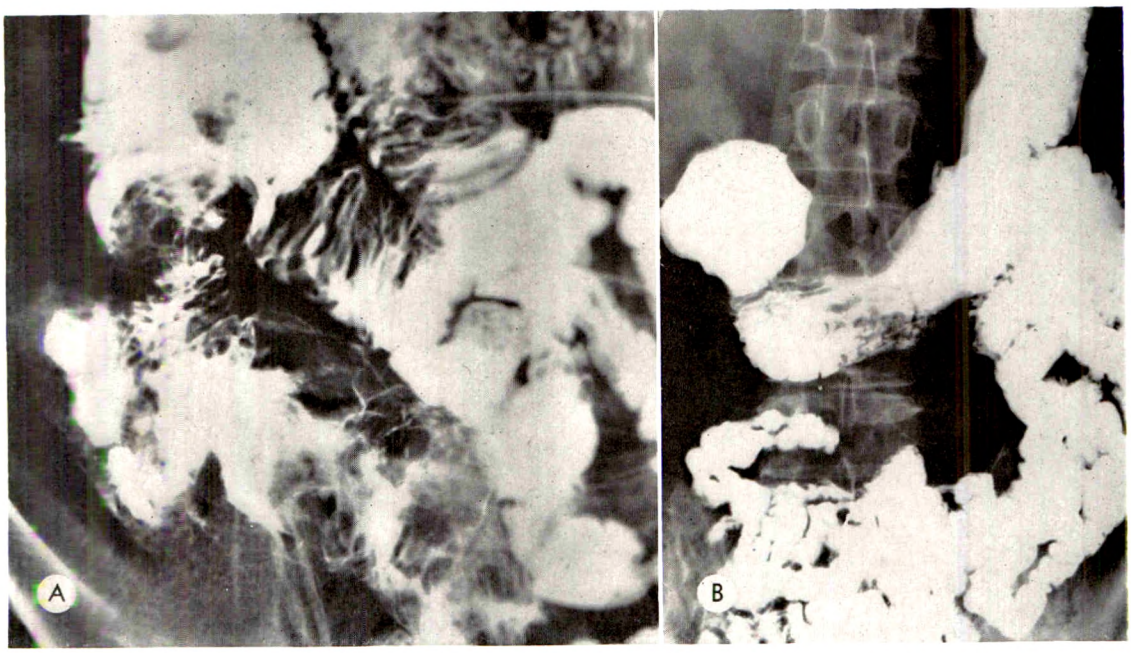


FIG. 8. (*A*) A markedly disorganized pattern produced by multiple polypoid masses with excavation, dilatation and numerous sinus tracts. (*B*) The duodenal bulb is replaced by a large amorphous irregular crater.

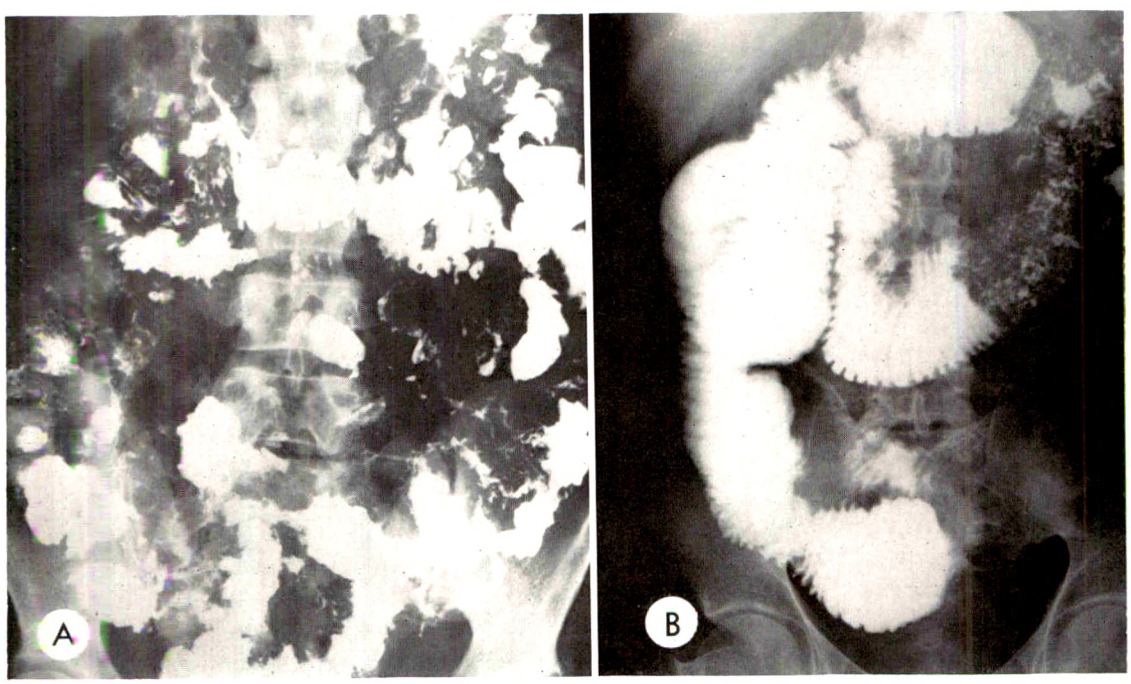


FIG. 9. (*A*) Diffuse lymphosarcoma of the mesentery and retroperitoneum, mimicking the sprue pattern, manifested by segmentation, hypersecretion and flocculation of the barium column. There is no evidence of intrinsic involvement of the bowel wall. (*B*) Unusual instance of obstruction produced by kinking and spasm at the site of an ulcerated intraluminal lymphosarcoma. The lesion was flat and, in itself, did not compromise the bowel lumen.

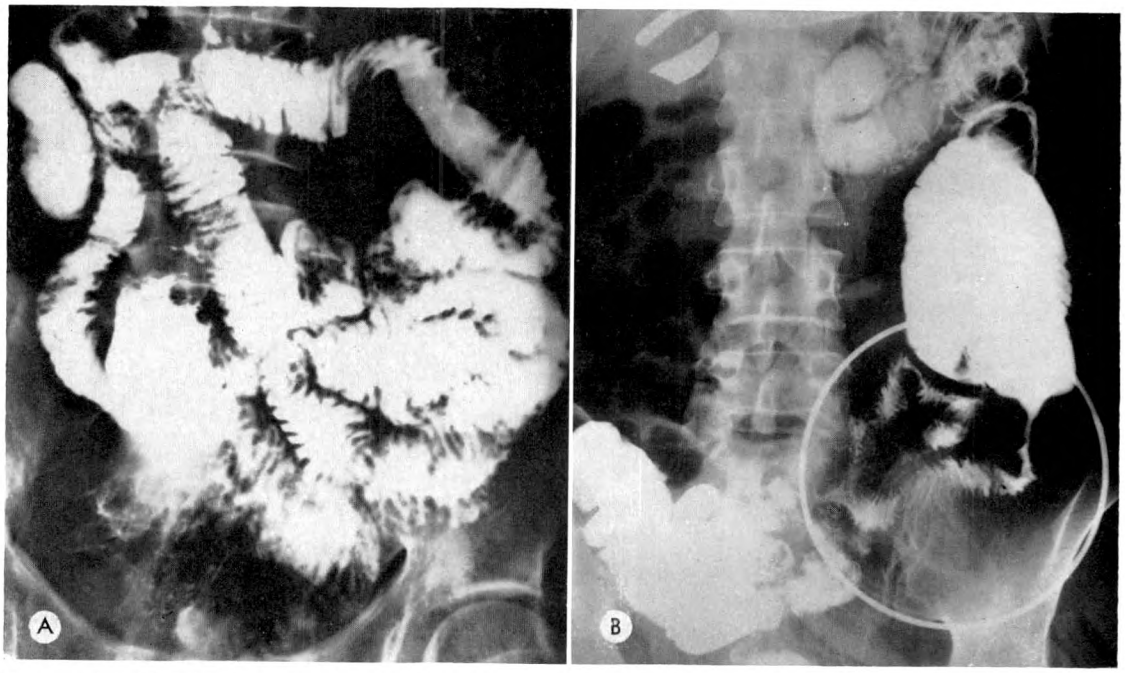


Fig. 10. (*A*) Hodgkin's disease. There are two segments of involvement. Proximally, the lesion simulates a long carcinoma except for lack of obstruction and proximal intestinal dilatation. Distally, the more usual characteristics of a lymphoma are seen with dilatation and perforation. (*B*) Hodgkin's disease of the jejunum. There is a narrow rigid segment producing obstruction to the barium column and dilatation. The contours are scalloped. No overhanging margins are seen. The lumen is eccentric. There is a fairly gradual transition between normal and abnormal bowel.

been as common. Differing from lymphosarcoma, Hodgkin's disease can produce marked fibrosis of the bowel wall with constriction of the lumen. Roentgenographically, there is eccentric narrowing of the bowel lumen, which tapers in a fusiform manner. There are no overhanging edges at the margins of the lesion, which is usually longer than that seen in carcinoma. The contour of the bowel lumen is irregular due to nodularity of the bowel wall. The involved segment may be fairly long. The sprue pattern, multiple small nodular defects and the infiltrating forms have all been seen in Hodgkin's disease. We have seen a single case of leukemic infiltration of the small intestine which appeared as multiple small nodular defects within a short small intestinal loop.

2. *Multiple polyps in the small intestine.* These are rare. When seen, they are usually one of the manifestations of Peutz-Jaeger's syndrome.

3. *Infarction of the small intestine.* An infarcted bowel segment shows progressive changes leading to stricture formation. The findings are similar to those of a benign stricture in other portions of the gastrointestinal tract, namely, a rigid, stenotic segment with a concentric lumen, the margins of which gradually widen to the caliber of the normal adjacent bowel. The margins are exquisitely smooth. Dilatation of the small intestine proximally occurs.

4. *Carcinomas.* These lesions are more common in the jejunum. They are usually short and cause an eccentric rigid lumen, the mucosa of which shows destruction and, occasionally, ulceration. The margins of the lesion are overhanging and obstruction is frequent. The lesions are usually single.

5. *Carcinoids.* Carcinoids occur more frequently in the distal ileum than in other regions of the small intestine. They have the same general appearance as carcinomas. However, on occasion, they may appear as

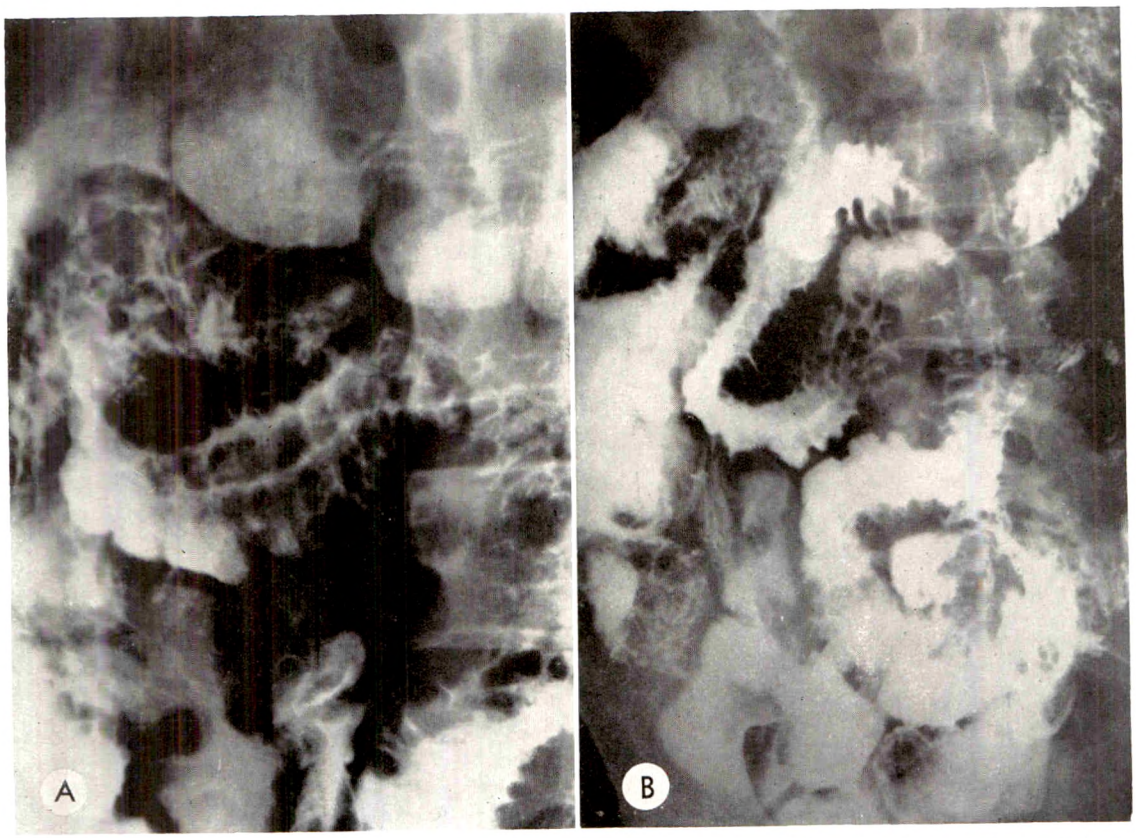


Fig. 11. (*A*) Regional enteritis, nonstenotic form. The mucosal folds are thickened and somewhat nodular in configuration. Linear ulcerations can be identified. (*B*) After an interval, inflammatory polyps appear which vary from tumor nodules in that they are fairly uniform in size, regular in appearance and intraluminal.

a conglomeration of nodular filling defects with some dilatation of the bowel lumen or as multiple isolated nodules with fixation and angulation of the adjacent bowel.

6. *Regional enteritis* (Fig. 11, *A* and *B*). Two thirds of these cases involve the distal ileum. The inflammatory process is characterized by fairly long segments (from 6 to 8 inches to the entire small intestine) of involvement which show linear mucosal ulcerations, inflammatory polyps, fistulas, sinus tracts, separation of the bowel loops due to thickening of the bowel wall and intervening mesentery, skip lesions, spasm, irritability and hypersecretion. On occasion, the nonstenotic phase of regional enteritis can simulate the appearance of diffuse lymphosarcoma of the small intestine. Thickening and blunting of the folds, irregularity of the contour, and intraluminal nodules are features which are common to both. However, in regional enteritis there is more inflammation, producing spasm and narrowing of the bowel lumen.

CONCLUSION

It is always easy to construct a classification and say that this is how to diagnose a particular entity. The small intestinal manifestations of lymphosarcoma are not common and, in their initial stages, are often missed. This has happened to us frequently and re-examination several months later because of persistent symptoms has shown obvious structural abnormalities in the small intestine. There is no doubt that these changes are not always as clear cut as they have been made to seem. On the other hand, in the literature

the prevalent feeling has been that it is rarely possible to diagnose small intestinal lymphosarcoma from roentgen study. This may be so in the individual case where the diagnosis may be extremely difficult. Nevertheless, study of a large number of these cases indicates that the diagnostic outlook is not as bleak as has been considered. The presence of lymphosarcoma can be suggested in a large percentage of cases. It is hoped that, with further study, the earlier changes will be recognized, perhaps altering the grave prognosis of this condition.

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ROENTGEN DIAGNOSIS OF LYMPHOSARCOMA AND RETICULUM CELL SARCOMA IN INFANCY AND CHILDHOOD*

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WHILE the roentgen findings in acute leukemia, neuroblastoma and other of the more common tumors and tumor-like lesions of the young appear to have been fully reported, a similar evaluation of generalized lymphosarcoma and reticulum cell sarcoma apparently does not exist. In fact, only in scattered reports and short references does one find mentioned the various roentgen appearances encountered in this relatively common group of neoplastic diseases of childhood.[5,7,12,17,18,20,28,30,32]

The roentgen diagnosis of lymphosarcoma and reticulum cell sarcoma in adults has been discussed in regard to involvement of bone,[26] thoracic contents[23,31] and the gastrointestinal tract, especially the stomach[16] and small bowel.[9] Because of the somewhat different clinical features these diseases display in children,[24] and in view of the special problems of differential diagnosis which in this age group face the roentgenologist, a more thorough and integrated approach to the roentgen identification of lymphosarcoma and reticulum cell sarcoma in infancy and childhood would seem to be indicated.

MATERIAL

Sixty charts filed under the designation of lymphosarcoma and reticulum cell sarcoma of patients 12 years of age or younger were first reviewed. These were in the period from January 1, 1928, to June 1, 1958. Only cases having histologic proof of lymphosarcoma, reticulum cell sarcoma or follicular lymphosarcoma and having one or more negative bone marrow aspirations were accepted. Consequently, the records of 23 patients who had lymphosarcoma but who also had or developed leukemia were excluded. All acceptable cases had adequate roentgenographic coverage. The total number of patients finally considered suitable for this study was 37. Twenty-four had lymphosarcoma; 12, reticulum cell sarcoma; and 1, follicular lymphosarcoma. Included were 2 patients considered by us to have so-called primary reticulum cell sarcoma of bone.

There were 26 males and 11 females. The mean age at the onset of the disease was 6.2 years with a range from 2 to 12 years. The mean survival rate was 22.3 months, with limits from 1 to 120 months. Ten of the patients are still living. Three of these are living 5.25, 7 and 10 years, respectively, and all are free of disease at present. Eight survived 4 years or longer. Eleven of the 27 patients who died were autopsied.

The diagnosis of lymphosarcoma and reticulum cell sarcoma is, of necessity, a pathologic one, with clinical recognition usually being made possible on the basis of exclusion of other diseases. The diagnosis in these cases was made from biopsy or autopsy material, and all of the histologic slides have been recently reviewed by a staff member of the Department of Pathology. Most of these patients were included in the excellent clinical review of lymphosarcoma in children by Rosenberg *et al.*[24] As they did, we use the term "lymphosarcoma" hereafter to cover the three entities mentioned.

As determined from all possible sources of reliable information, *i.e.*, physical and roentgenographic examinations, biopsy, surgical and postmortem examinations, the

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sites of disease which were identified at one time or another during the course of the illness in the 37 cases are as follows: lymph nodes 25 (cervical 15, mediastinal 16, retroperitoneal 15); pleura 5; bone 10; genitourinary tract (other than kidney) 4; kidney 10; lung 3; gastrointestinal tract 16 (intussusception 6); pancreas 5; gallbladder 2; adrenal gland 3; heart and pericardium 2; tonsil 2; thyroid 2; skin 1; central nervous system 1; adenoids 1; nasopharynx 1; parotid gland 1.

A correlation of these areas of involvement by lymphosarcoma with the ones that were revealed roentgenologically indicated that the radiologist was capable of demonstrating the majority of the lesions by roentgenologic methods. Consequently, the importance of thorough roentgen examination, followed by careful interpretation, is readily apparent in lymphosarcoma.

Charache[3] reported that lymphosarcoma comprised 6.3 per cent of 1,800 malignant tumors in children reported from 7 institutions and 11 per cent of malignant tumors in children studied at the Brooklyn Cancer Institute over a 22 year period. Dargeon[8] noted that lymphosarcoma comprised 5 per cent of 583 malignant tumors in children treated at Memorial Hospital from 1926 to 1950. These compilations and others demonstrate that lymphosarcoma in childhood is not an uncommon form of neoplastic disease.

Rosenberg *et al.*[24] found that the 5 year survival rate in 69 children was 17.4 per cent. Stout[29] observed that in most patients lymphosarcoma may spread rapidly, but occasionally the progress is slow and the disease remains localized for a long period of time. Of 119 cases of lymphosarcoma he reported 12.7 per cent were symptom free after 10 years. Other investigators, Craver,[6] Diamond,[10] Eisenoff *et al.*,[11] Dargeon,[8] Rhoads,[21] and Charache,[3] have reported a few apparent cures. Stout[29] and others[6,8] have emphasized that, when the disease is localized (in other words, when the diagnosis is made early), the response to treatment and the prognosis are better. This points up the importance of roentgen diagnosis in detecting small and early areas of tumor involvement.

ROENTGEN FINDINGS

There were 4 of the 37 patients whose roentgen examinations were negative. These examinations covered the chest, abdomen and bones and the studies spanned periods of time up to 4 years. All 4 patients had local disease in the neck and all are now living.

BONES

The roentgen examinations carried out on the 37 patients revealed 9 with involvement of the osseous system. The bone disease was in 2 categories. Two cases seemed consistent with primary reticulum cell sarcoma of bone,[19] while the larger number was thought to have the generalized type of disease. Cases considered acceptable as primary reticulum cell sarcoma of bone must show no evidence of tumor disease other than the single lesion of bone, as far as can be determined by all appropriate methods of examination. In addition, patients must fail to develop the disease elsewhere for a period of at least 5 months. In a group of 17 cases of this form of the disease previously reported,[26] the youngest patient was 13 years of age and most were 20 or older.

One case of primary reticulum cell sarcoma of bone roentgenographically showed a "mixed type" lesion, *i.e.*, equal amounts of bone lysis and sclerosis (Fig. 1). After radiation treatment, the process became denser and more sclerotic. The second case having a "mixed type" roentgen appearance with periosteal reaction occurred in the distal femur, and it too showed improvement with the development of more sclerosis after irradiation.

Two of the patients having the generalized form of bone involvement presented findings somewhat resembling those commonly encountered in leukemia due to the symmetric distribution of bone destruction in the metaphyseal regions. Both had negative marrow aspirations for leukemia at the

time of the bone invasion. One also presented a localized area of destruction in an os calcis. The transverse bands of diminished density at the metaphyses seen in acute leukemia were absent and the extensiveness of the destruction as well as the degree of sclerosis were both considered to be unusual for leukemia (Fig. 2). Apparently, however, a leukemic type of bone involvement can sometimes be found in patients with generalized lymphosarcoma.

Two children with lymphomatous disease elsewhere showed single osteolytic defects resembling cancer metastases. In another, the involvement was irregularly placed in many bones and was of the "mixed type," while in still another the scattered lesions were slightly sclerotic. The last case, which some might qualify as a primary reticulum cell sarcoma of bone, also showed the "mixed type" roentgen appearance.

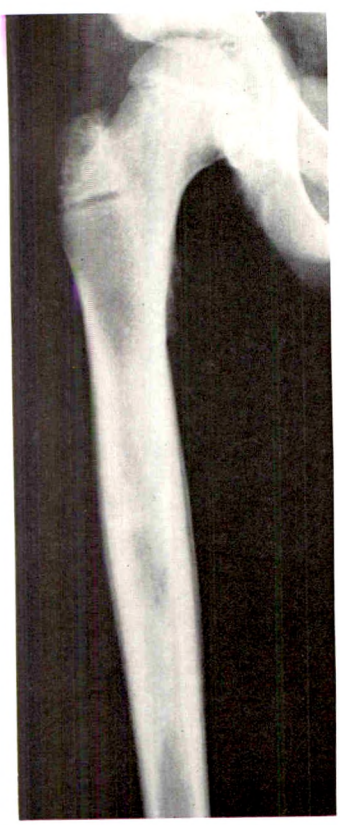


Fig. 1. F.O. Primary reticulum cell sarcoma of bone. Solitary, "mixed type" lesion in the femoral shaft. The disease did not become generalized until four years later.



Fig. 2. P.G. Symmetric involvement at the metaphyses of all the large long bones.

This information discloses that the roentgen findings of lymphosarcoma of bone, whether of the primary or secondary variety, are not diagnostically specific. However, as has been pointed out previously,[26] the possibility of this disease being present is suggested when certain roentgen findings are encountered. The hit-and-miss character of the bone involvement, along with evidence of neoplastic involvement in other consistent sites such as lymph nodes, kidneys and gastrointestinal tract, will often suggest the correct diagnosis of generalized lymphosarcoma.

KIDNEY

Two of the 10 patients with known lymphomatous disease of the kidney had no roentgenograms of the urinary tract or abdomen. Six of the 8 who had roentgeno-

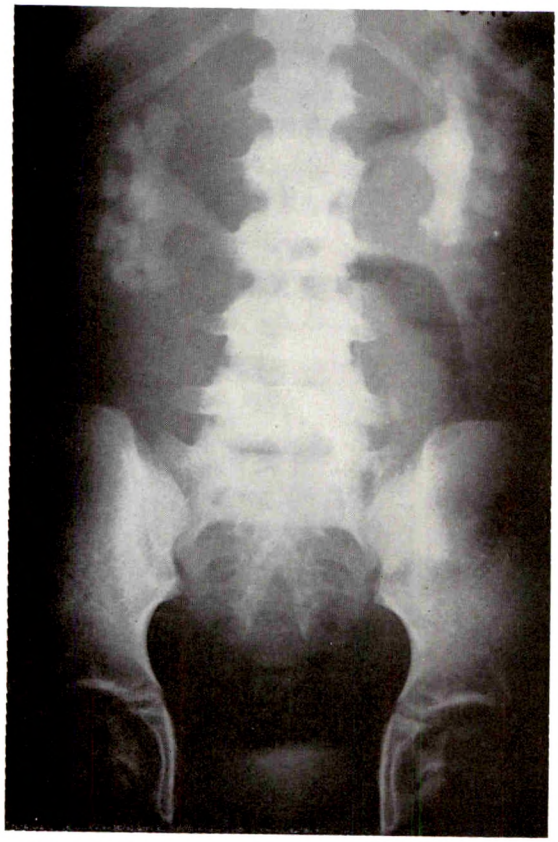


Fig. 3. S.S. Marked symmetric enlargement of the kidneys, particularly in the cortical zones.

graphic examination showed bilateral, more or less symmetric enlargement of the kidneys. The enlargement was usually moderate in degree, the kidneys appearing 2 to 4 times their normal size. Most of these patients had more than 1 excretory urographic examination. Two with scout roentgenograms of the abdomen only and 1 with an excretory urogram showed some degree of loss of the kidney outline due to either ascites or massive intraabdominal disease. Obstruction of one ureter and failure to identify any kidney outline were other roentgen findings.

As seen on the pyelographic studies the typical roentgen appearance of lymphosarcomatous invasion was bilateral, fairly symmetric enlargement of the kidney silhouettes, a relative widening of the cortical area and some slight lengthening and thinning of the infundibula of the minor and major calyces. There was no significant alteration in the appearance of the kidney pelvis (Fig. 3). A localized defect marked by local calyceal deformity and enlargement with absence of function developing later presented the only instance of a bulky solitary defect of the kidney due to the tumor. The roentgen appearance in the majority, therefore, bore a close resemblance to that in children with acute leukemia, as has been described.[15]

The patients with kidney involvement had negative laboratory tests for urinary tract disease. In 1 instance, the enlargement disappeared entirely following treatment, the kidneys taking on a normal roentgen appearance (Fig. 4, *A* and *B*). This improvement took place within a 9 month interval. We have observed generally similar roentgen findings and a similar response following therapy in adults.[22]

Lymphosarcomatous involvement of the kidneys in the young must be differentiated roentgenologically from bilateral polycystic disease. The relative widening of the cortex and the absence of any striking degree of calyceal alteration both favor lymphosarcoma. Also, the kidney outline shows no lobulation and the pelvis is not deformed. Response to local irradiation or systemic treatment takes place with lymphosarcoma. Obviously, it is impossible to distinguish roentgenologically between leukemic and lymphosarcomatous disease of the kidneys.

A survey of the literature dealing with lymphosarcomatous involvement of the kidneys revealed only a few reports. However, Ewing[13] found in postmortem examinations that the kidney is a favorite site for lymphosarcoma. He noted that "the deposits may take the form of minute foci, bulky masses or diffuse infiltration." Baldridge and Awe[1] reviewed 150 cases of lymphoma but reported only 1 with lymphosarcoma of the kidney proved histologically. Excretory urography was not done on this patient. Gowdey and Neuhauser[15] reported on 3 cases of acute lym-

phocytic leukemia with kidney involvement. The kidneys, as revealed by excretory urography, showed symmetric and generalized enlargement. Histologically, the nephrons were separated by massive leukemic infiltration, primarily of the cortex. Barney[2] noted kidney involvement in 18 of 23 cases of lymphoblastoma of the urinary tract coming to autopsy. No urographic examinations were done on any of these patients. Freifeld[14] reported a case of lymphoblastoma of the kidney in a 17 year old male. However, this patient had 50 per cent immature cells in the peripheral blood and similar cells also were numerous in the bone marrow. On excretory urography, the kidneys were found to be generally enlarged and microscopic examination at autopsy showed infiltration of the cortex with leukemic cells.

The gross pathologic description of the kidneys in this series was summarized for us by Dr. Stephen Sternberg of the Department of Pathology. He stated that in lymphosarcoma there was no single characteristic or uniform pattern of kidney involvement. However, small and numerous nodular deposits seemed to predominate, although a few times a somewhat localized or bulky mass was found.

LIVER AND SPLEEN

Enlargement of the liver and spleen were noted roentgenologically only 3 times. Enlargement of the spleen only and of the liver only was present once. The roentgenologist sometimes is able to detect splenic enlargement not clinically evident, because splenomegaly can assume a more or less spherical form, rather than the usual downward enlargement which makes the lower pole easily palpable. However, somewhat to our surprise, it appeared that neither splenomegaly nor hepatomegaly were particularly helpful signs in identifying lymphosarcoma in the young.

LYMPH NODES

Almost 50 per cent of the patients showed

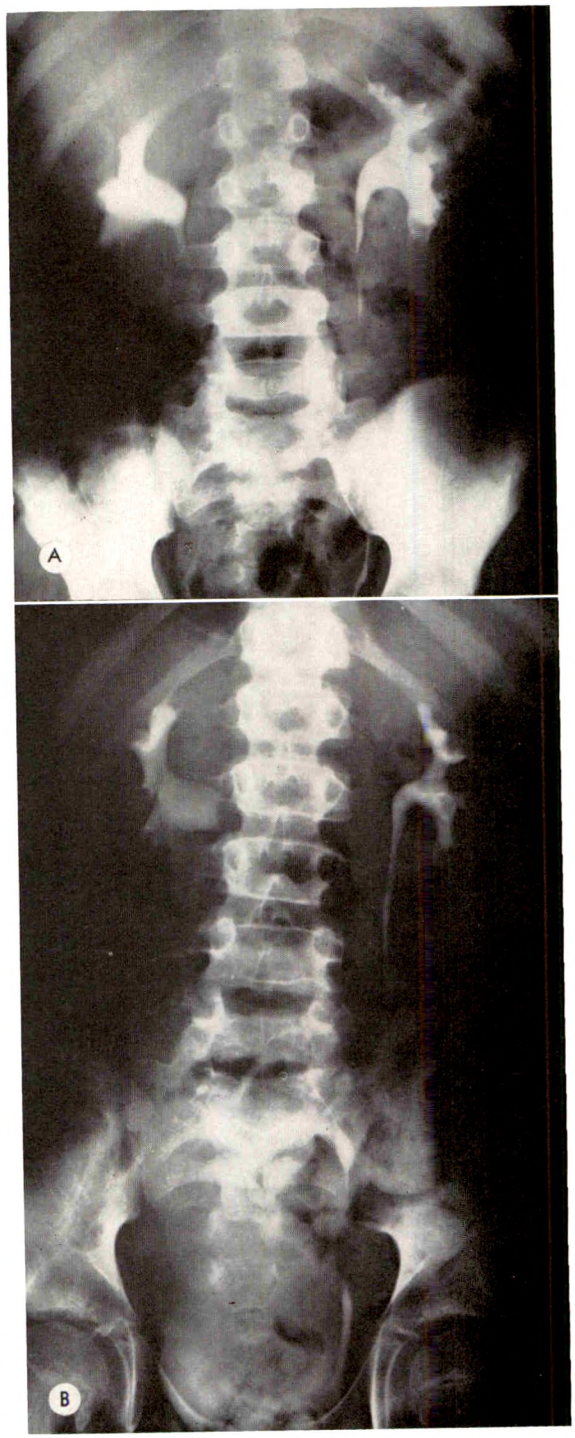


FIG. 4. G.C. (*A*) Moderately and symmetrically enlarged kidneys, July 23, 1956. (*B*) Almost normal appearance after treatment, May 8, 1957.

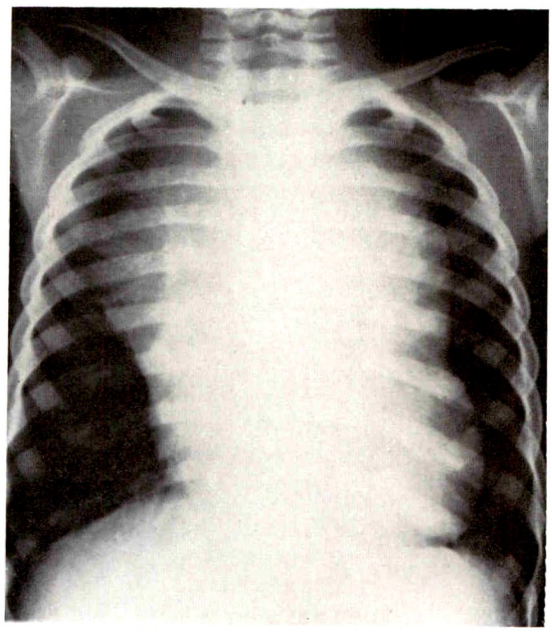


Fig. 5. R.G. Large mediastinal mass due to lymphosarcoma.

roentgen evidence of lymph node enlargement. This was usually in the chest, particularly in the mediastinum (Fig. 5). The roentgen characteristics of lymphoblastomatous involvement in the lymph nodes of the thorax in adults have been thoroughly described and need not be reviewed here. The findings in children are similar.

The abdomen was the next most common site of lymph node enlargement detectable roentgenographically. In confirming this form of lymphosarcoma, a previously negative scout roentgenogram for reference is of great value. Good technique is a major requirement. Obscuration of organ outline, areas of increased density and displacement of known structures are the chief alterations to search for as indicative of lymphadenopathy. Generally speaking, the roentgenologic examination is extremely helpful and in fact a necessity in the evaluation of abdominal masses in children.

Following the scout roentgenogram of the abdomen, the next logical step in the roentgen appraisal of the abdomen in lymphosarcoma is excretory urography. Minor alterations in the position and course of the ureters as seen in the sagittal projection should be interpreted with some caution, because by tracing normal ureters we have found that a fairly wide variation is possible. An abrupt deviation usually is more significant than a smooth, general deviation from the expected normal. Next, the gastrointestinal series, with particular attention to the position and contour of the duodenal loop, may be helpful. Retroperitoneal air injection, aortography and similarly complex studies do not seem to be indicated in children with malignant lymphomas.

Abdominal fluid was suspected in 7 cases, pleural effusion in 5, and in 4 fluid was thought to be present in both of these body cavities.

GASTROINTESTINAL TRACT

The greater incidence of gastrointestinal tract invasion in children as compared to adults has been pointed out.[24] Ten patients roentgenologically showed one or more areas of lymphosarcoma in the gastrointestinal tract. Usually the lesions were polypoid and infiltrating in character, giving the roentgen appearance of cancer (Fig. 6). One aspect to be emphasized is the fre-

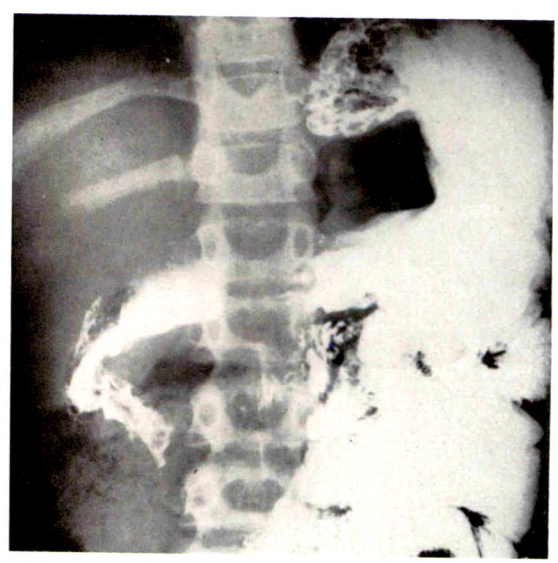


Fig. 6. H.H. Involvement of the second portion of the duodenum. There was an accompanying mass in the right upper quadrant.

quency with which gastrointestinal tract involvement by lymphosarcoma presented as an emergency in this age group. There were 4 patients with intestinal intussusception (Fig. 7) who had roentgenograms available for study, and 2 additional patients presented this symptom complex.

LUNG

The lung is not infrequently involved by lymphosarcoma in adults, but only 5 of these young patients showed this feature as determined by the roentgen findings. Two had rather small, ill-defined, nodular infiltrates, while 3 presented a more patchy or bronchopneumonic-like pattern. Certainly nothing specific about the roentgen appearance of lung invasion by this group of neoplasms was noted (Fig. 8).

OTHER SITES

Some of the more unusual sites of disease were the nasopharynx, ovary, mandible, sphenoid bone and duodenum. In all these areas roentgen evidence of the cancer was present.

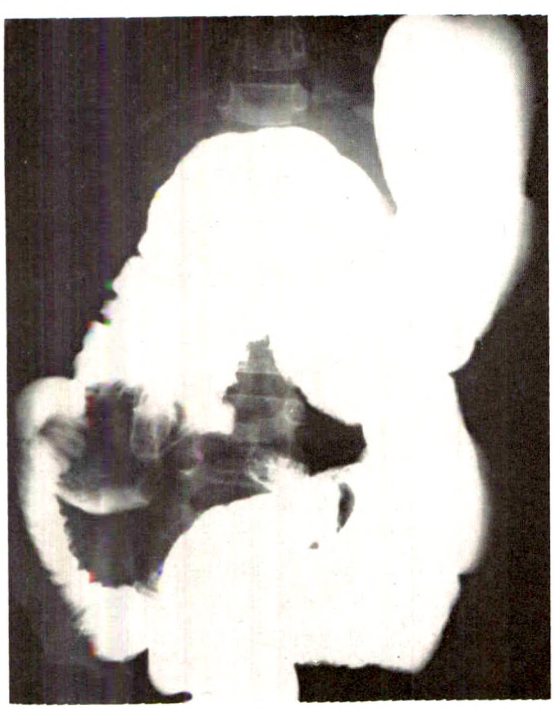


Fig. 7. N.T. A mass in the cecum and ascending colon with intussusception.

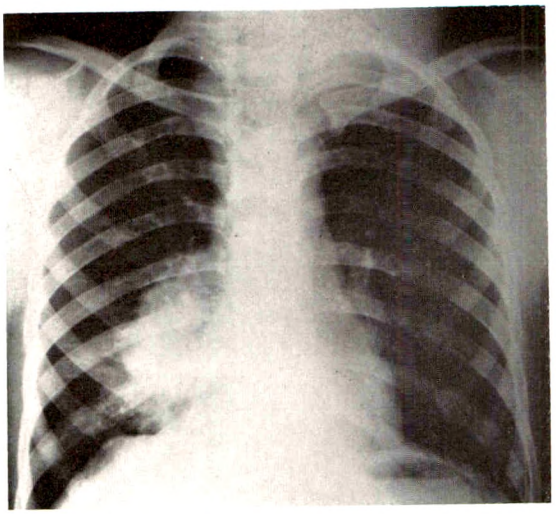


Fig. 8. J.A. An irregular mass in the right lower lung field with lymphadenopathy in the mediastinum and left lower cervical region.

DISCUSSION

There is very little that is specific in the single, localized deposit of lymphosarcoma, wherever it may be located in the body. The somewhat characteristic roentgen appearance in primary reticulum cell sarcoma of bone is encountered infrequently. The findings in the kidney are perhaps more helpful, as they are more often seen. A pattern of symmetric and generalized enlargement would seem to be highly indicative of lymphosarcoma when it is accompanied by roentgen evidence of tumor in other sites. If the kidney involvement is noted alone, then its close resemblance to leukemic invasion of the kidneys would make differentiation between these diseases impossible.

A main point in the roentgen diagnosis of lymphosarcoma, therefore, is that, while one must be acquainted with the appearance of the individual lesion as it involves various organs, the diagnosis is usually made more on the basis of the multiple sites of involvement and their irregular sequence and haphazard arrangement in the body.

Patients who exhibit localized lymphosarcoma clinically, *i.e.*, cervical or axillary lymphadenopathy, should have as a min-

imal roentgen examination a roentgenogram of the chest and a scout roentgenogram of the abdomen, in addition to a thorough study of the local area itself. For those with more widespread disease, skeletal survey, excretory urography and gastrointestinal tract examinations should be carried out. Furthermore, periodic studies of these various regions are indicated because of the tendency of lymphosarcoma to progress and appear in new sites. The chest, skeleton and abdomen are areas where a roentgen survey is most likely to uncover lymphosarcomatous involvement not readily apparent clinically.

Roentgenologically, a differential diagnosis from Hodgkin's disease would be impossible. However, the age limit in lymphosarcoma tends to extend somewhat lower, with Hodgkin's disease in childhood being less common than lymphosarcoma.

Neuroblastoma beginning in ganglionic tissue tends to act more like a primary malignant tumor than one of multicentric origin. Usually the primary site is the adrenal gland. In 40 per cent of the cases the primary focus roentgenologically shows calcification.[25] This fact plus the characteristics of the primary mass will often immediately distinguish this disease from abdominal lymphosarcoma. Calcification with a lymphosarcomatous deposit was not found in this series, even after treatment had been given. In neuroblastoma, the metastases to bone tend to be more frequent and widespread. They are usually symmetric and metaphyseal.[25] This is quite dissimilar to the irregularly scattered distribution of the bone lesions in lymphosarcoma. Generally speaking, therefore, when these two diseases are well advanced, their differential diagnosis is easy.

Wilms's tumor, with its primary involvement of one kidney and its tendency to metastasize to the lungs, yields quite different roentgen findings from lymphosarcoma. The renal findings particularly are conspicuous, because they are almost always unilateral and localized.

The osseous lesions typical of acute leukemia in children are not encountered in lymphosarcoma, although in an occasional instance a slightly similar type of involvement of the bones may occur.[27] It appears, therefore, that most cases of lymphosarcoma, particularly if multiple sites of involvement are present, would be readily distinguishable roentgenologically from acute leukemia.

SUMMARY

1. Thirty-seven proved cases of lymphosarcoma in children have been reviewed in order to determine the roentgen findings in this group of diseases.

2. The roentgen appearance of lymphosarcoma of the kidneys and of primary reticulum cell sarcoma of bone may at times suggest the diagnosis.

3. The correct roentgen diagnosis will usually rest upon the finding of multiple areas of tumor disease in several different organs and the irregularity and asymmetry of the involvement.

4. Children with known lymphosarcoma should always have chest and abdominal roentgenograms, regardless of the location of the primary site or how localized the disease seems to be clinically.

5. Once a bone lesion is detected in lymphosarcoma, a skeletal survey is indicated.

6. Generally speaking, lymphosarcoma, one of the more common neoplasms of childhood, can usually be distinguished roentgenologically from neuroblastoma, Wilms's tumor, leukemia and other neoplasms of childhood, particularly when these diseases are advanced.

7. Six of the cases with kidney disease revealed bilateral, symmetric renal enlargement in spite of negative tests for urinary tract disease and negative bone marrow examinations for leukemia.

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METASTATIC BREAST CARCINOMA SIMULATING ULCERATIVE COLITIS

REPORT OF A CASE

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IN A recent discussion,[14] a variety of types of involvement of the colon by metastatic lesions was presented. We have had occasion to examine the roentgenograms and pathologic specimens of a patient with metastatic disease to the large intestine which showed roentgenographic signs of inflammatory rather than of neoplastic disease.

REPORT OF A CASE

R.R. was a fifty-nine year old white woman who was admitted to the University of Minnesota Hospitals on November 11, 1957.

The patient had had a right radical mastectomy for carcinoma ten years previously. Two years later, because of metrorrhagia, a hysterectomy had been performed.

Five years before admission the patient had developed constant epigastric pain, intensified by heavy meals and relieved by aspirin. This subsided three years later. Diarrhea had then developed, with five to eight defecations per day. At the time of admission the patient was having five bowel movements daily, most frequently at night. There was no pain. Stools were described as watery, without blood or mucus.

For three years the patient had noticed increasing fatigue, weakness and anorexia with at least a fifty pound weight loss. About two weeks before admission she began to notice abdominal swelling and shortness of breath. Swelling of the left lower extremity had been present for one week. For several years she had noticed nodules in the skin.

Physical Examination. Vital signs were normal. The skin was pale. Numerous nodules, from 0.5 to 1.0 cm. in diameter, were scattered over the anterior and posterior trunk and upper arms. These were located predominantly on the right, in the area of the absent breast. Marked abdominal distention was present. There was a midline lower abdominal scar. A reducible hernia was present below the umbilicus. A hard, nodular mass could be palpated through the hernia superiorly and to the right. The mass was not movable and was thought to represent a tumor or intestine involved by tumor. The liver was not palpable. There was evidence of free fluid.

Laboratory Examination. Hemoglobin was 7.0 gm. per cent; white blood cells, 6,000, with a normal differential count; a stool specimen was grossly bloody.

Roentgen Studies. Chest roentgenograms showed an absent right breast, high diaphragm, and extensive osteolytic bone metastases but no pulmonary metastases. Roentgenograms taken during an examination of the colon at another hospital on June 8, 1957 were reviewed (Fig. 1, *A*, *B* and *C*). They were interpreted as showing changes throughout the colon consistent with long standing chronic ulcerative colitis.

Hospital Course. The patient was considered to have metastatic breast carcinoma, but the origin of the abdominal problem was in doubt. The most likely possibilities were metastatic breast carcinoma to the peritoneal cavity, metastatic ovarian carcinoma, or carcinoma of the colon secondary to ulcerative colitis. Therapy consisted of paracentesis, cortisone and stilbesterol. A skin nodule was excised and reported as "metastatic carcinoma of the chest wall, which is of glandular origin and resembles the scirrhous type." Bloody diarrhea continued and because of the onset of hematemesis steroid therapy was halted. Blood transfusions were given as required. The patient continued to decline and expired on December 1, 1957.

Autopsy Findings. Subdermal metastases were noted, many of which were near the mastectomy scar.

Peritoneal carcinomatosis was quite striking. About 75 per cent of the stomach wall was thickened, showing the picture of linitis plastica. There were, in a particularly thickened area just proximal to the antrum, two punched out areas of ulceration in the gastric mucosa, the larger measuring 8 mm. The colon showed a "lead pipe" configuration, having very straight

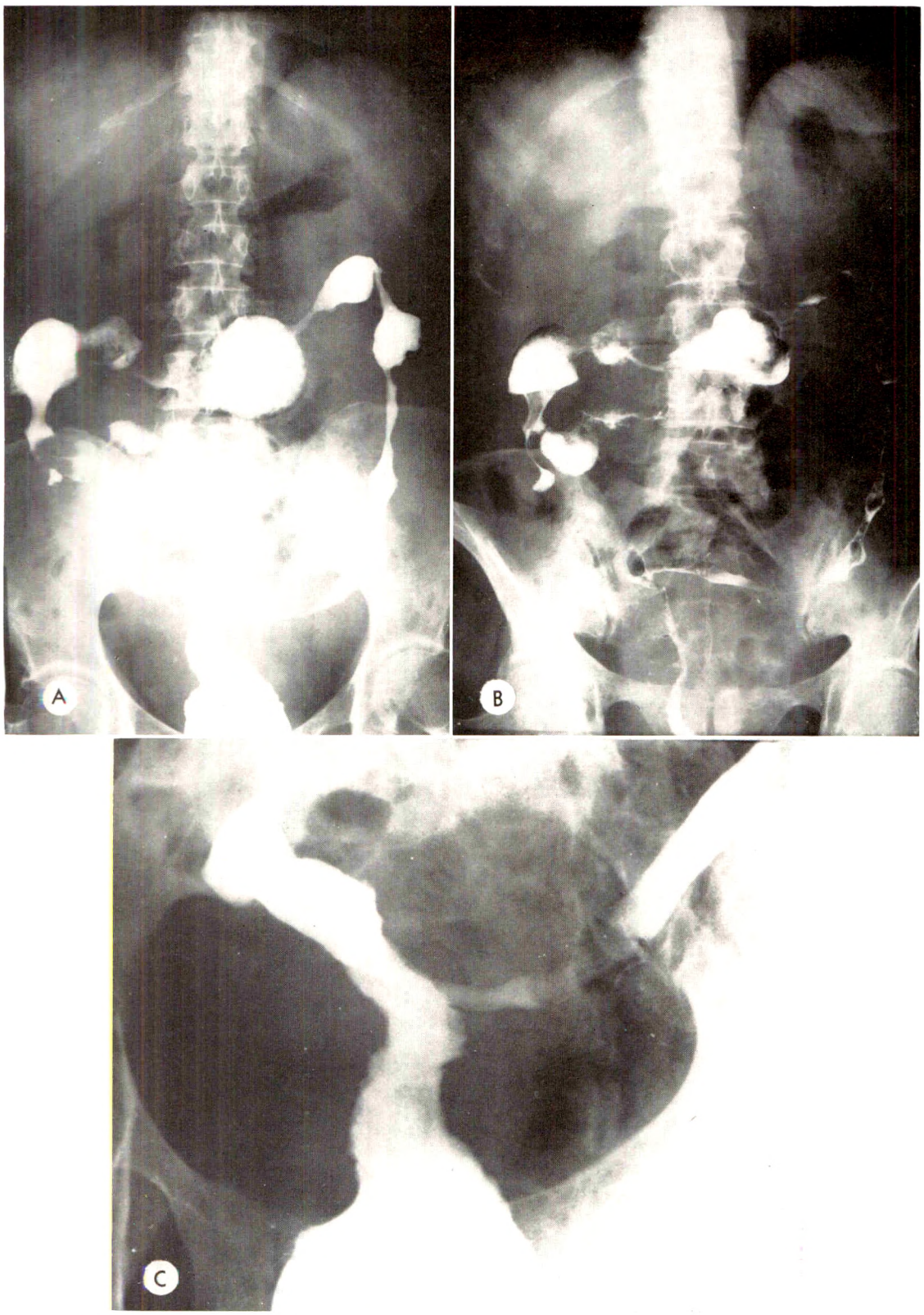


FIG. 1. (*A*) Pre-evacuation and (*B*) post-evacuation roentgenograms of the colon. (*C*) Spot roentgenogram of the rectosigmoid. Typical changes of ulcerative colitis are demonstrated. Note the "ulcerations" in *C*. Lytic bone metastases are present.

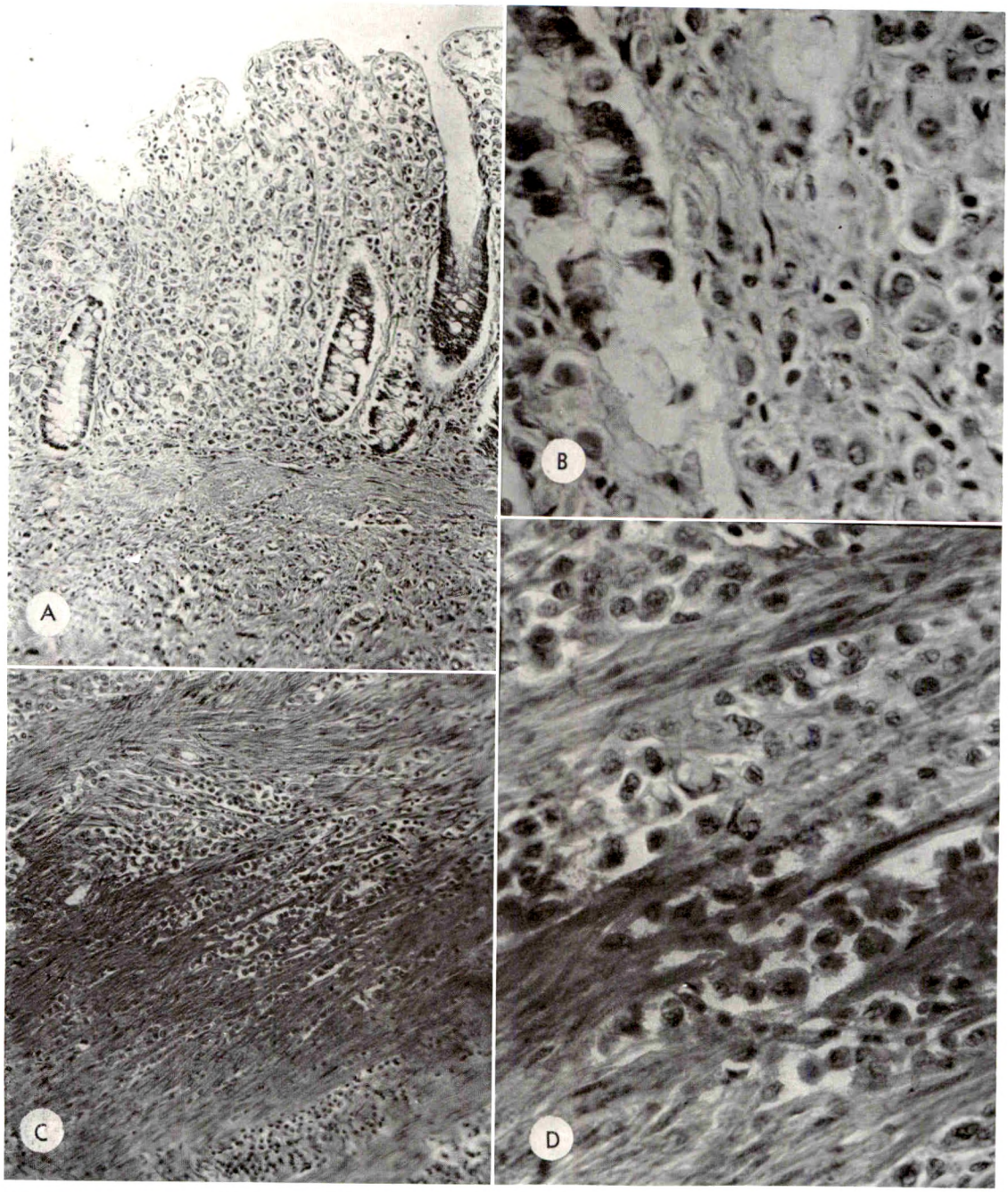


FIG. 2. Photomicrographs of sections of the colon: (*A*) mucosa, ×100; (*B*) mucosa, ×440; (*C*) muscularis, ×100; and (*D*) muscularis, ×440. Note the diffuse tumor cell infiltration of the mucosa and muscle. There are persisting normal glands which are autolyzed but do not show the changes of ulcerative colitis.

and obviously shortened segments. The lumen was small, approximately 1 cm. in diameter throughout, but the wall was markedly thickened, up to as much as 8 mm., from the cecum to a point well below the peritoneal reflection. The mucosal lining appeared smooth and shiny.

The microscopic changes in the colon (Fig. 2, *A–D*), stomach, and bladder were quite comparable in that each showed diffuse infiltration of the mucosa, submucosa and muscle by malig-

nant epithelial cells, for the most part separate one from the other. Some of the tumor cells contained cytoplasmic vacuoles which displaced the nucleus to one side to form "signet-ring" cells. None of the colon sections showed changes compatible with ulcerative colitis.

Other sites of metastases included numerous lymph node chains, the left breast, visceral pleura, liver, spleen, left kidney, bladder, peritoneum retroperitoneum, bone marrow and right ovary. There was bilateral hydronephrosis, more marked on the left, apparently related to external ureteral compression by neoplastic involvement of the retroperitoneum.

DISCUSSION

Lesions of the colon having the gross appearance of linitis plastica and a microscopic picture of diffuse epithelial tumor cell infiltration of the mucosa, submucosa and muscle have been described. Our perusal of the literature revealed 5 such lesions interpreted as primary carcinoma in the colon[7,13] and 17 interpreted as unusual metastases from gastric carcinomas of the linitis plastica type.[1,3,4,6,9,11,12] Only 4 cases have been described which, in our opinion, represent metastatic carcinoma to the colon from the breast.[3,4,5]

In 1909, Faroy[2] probably noted the first such case, a forty-one year old woman who had had vague gastric complaints for one year. At autopsy there was a 6 cm. hard mass, which was fixed to the skin, in the right breast. There were numerous subcutaneous nodules as well. The colon showed some patchy areas of narrowing associated with thickening of the wall, while the stomach grossly demonstrated striking thickening of the walls. The microscopic examination of the stomach, the only organ studied by microscopy, showed neoplastic cells in the mucosa and submucosa.

The second case described as metastatic carcinoma from the breast was that of Jørgensen in 1935.[5] His patient showed a linitis plastica pattern in the stomach, segments of the colon, the ureters and the rectovaginal septum. Microscopically, he found these tissues, as well as the myocardium, infiltrated by large, well-circumscribed, tumor cells. He stressed that these cells stained positively with mucicarmine and infiltrated the involved structures without producing a significant reaction in the surrounding tissue.

Fischermann[3] has recently described 2 other cases of metastatic carcinoma of the breast, one infiltrating the muscle of the stomach and the second the muscle layers of the stomach, rectum, sigmoid colon, uterus, and uterine tubes. In each of his cases the patient's chief complaint was some variant of "dyspepsia." Jørgensen's patient, too, in addition to noticing the presence of a breast mass, complained first of fatigue, diarrhea, and "gastric influenza," with vomiting, at least fourteen months before her death. In Fischermann's second case a colostomy had been performed nine months prior to death for what was mistakenly thought to be a primary carcinoma of the rectum. In our case also, the patient had had diarrhea for three years prior to death, that complaint being, in retrospect, the first definite sign of metastatic carcinoma.

The roentgenographic findings in this instance very accurately simulated those of advanced ulcerative colitis, namely, loss of the normal mucosal pattern, loss of haustral markings and decrease in the size of the colon, both of the lumen and the over-all length. A variation of the shortened, narrowed colon, called the "linked sausage appearance" in Bockus' text,[10] was also seen in this case. Interestingly, though the roentgen appearance was that of multiple, minute ulcerations, especially demonstrated on the spot roentgenogram of the rectosigmoid, none were actually present. Presumably, this roentgen finding was produced by the fixed buckling of the mucosa secondary to the involvement of the entire thickness of the colonic wall by metastatic tumor.

Similar roentgen appearances of linitis plastica in the colon have been reported. In the first case of Laufman and Saphir[7] there had been a long (twenty-three year) history

of ulcerative colitis. Therefore, though the pathologic findings were of diffuse scirrhous carcinoma, it would have been impossible to determine whether the colitis or the carcinoma caused the roentgen changes. Karstens and Bargen[6] reported 2 cases without a clinical history of ulcerative colitis that showed roentgen findings of ulcerative colitis. In both, operation revealed extensive scirrhous carcinoma involving the stomach and colon. On a statistical basis it was likely that the primary disease was in the stomach in both cases. Sussman[12] similarly reported 2 cases of coincident carcinoma of the stomach and colon with the primary most likely in the stomach.

Our case, then, might represent a primary carcinoma of the stomach, colon or breast. The over-all duration of the patient's disease and the appearance of nodules in the skin, some in the mastectomy scar as well as in distant sites, support the premise that this was primary in the breast, especially since there was a history of breast carcinoma. Thus, this is the fifth reported case of metastatic carcinoma from the breast with the unusual clinical, roentgenologic and morphologic changes described.

SUMMARY

A case of metastatic carcinoma of the breast with unusual visceral metastases is described. The roentgenologic changes in the colon are indistinguishable from those of chronic ulcerative colitis.

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We wish to thank Dr. James R. Dawson and Dr. Harold O. Peterson for their valuable criticism and suggestions. This case is published with the permission of Dr. B. J. Kennedy of Minneapolis and Dr. J. P. Medelman of St. Paul, Minnesota.

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NEW ROENTGENOLOGIC SIGNS OF CARCINOMA OF THE URETER*

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IN PYELOGRAPHY, as so often happens in clinical medicine, no absolute yardstick exists by which to differentiate minor variations of normal from minor or early changes of the abnormal. We are forced to evaluate the variations in each segment of the urinary excretory tract and try to determine whether the minor alterations seen on roentgenograms are significant enough to support the presumptive clinical diagnosis.

Our study is an attempt to evaluate the present concepts for early diagnosis of ureteral carcinoma, and to illustrate certain specific changes which we have found helpful.

When faced with a patient presenting the clinical symptoms of painless or recurrent hematuria, it must be axiomatic that the intravenous pyelogram must not be considered normal unless the entire ureter is completely and satisfactorily visualized from the renal pelvis to the ureterovesical junction. The greatest cause of misdiagnosis is the labeling of an intravenous pyelogram as normal when the entire ureter is not visualized; what appears to be an area of peristalsis may, in fact, be a ureteral defect.

In our series, we have seen 4 apparently normal intravenous pyelograms on which the ureter above and below the lesion revealed no evidence of dilatation, but at the site of the lesion a short segment of the ureter was not visualized. For an adequate evaluation retrograde pyelography must be performed when space defects in the ureter are observed on intravenous pyelograms.

We would like to present two findings of carcinoma of the ureter not previously emphasized:

1. The kidney and ureter above the site of the ureteral tumor may be entirely normal. Most textbooks[3,5] emphasize the presence of severe hydronephrosis or a nonfunctioning kidney as the primary finding in ureteral carcinoma. The degree of hydronephrosis is simply an expression of the degree of obstruction produced by the lesion and therefore small and occasionally large lesions may produce almost no ascending obstruction. One cannot correlate the degree of obstruction with the size of the tumor but, in general, later stages of the disease will be more likely to present obstruction. In our series, as previously stated, approximately one-half of the cases presented normal appearing upper urinary tract and ureters on intravenous pyelograms.

2. On the retrograde study, we have observed a peculiar coiling of the catheter which occurred just below the site of the lesion. The mechanism of this coiling will be explained later.

In a previous publication[1] we noted that with the development of more adequate diagnostic techniques, the clinical recognition of ureteral tumors has become less difficult. Primary neoplasms of the ureter, formerly considered rare, have been recognized in ever increasing numbers.[11] Senger and Furey[9] state that 86.5 per cent of tumors of the urinary epithelium occur in the bladder, while 8.4 per cent occur in the renal pelvis and ureter. Foord and Ferrier[2] calculate that about 1 per cent of carcinoma in the upper urinary tract originates in the ureter.

In the history of this lesion, Rayer of France described the first case in 1842; however, it was not till 1878 that the first

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histologically proved case was reported by Wising and Blix. As recently as 1934[4] only 68 acceptable ureteral malignancies were reported, but by 1955 this number had risen to 333 as reported by Savignac.[7] It is safe to assume that the present number is well over 500 cases.

Seventy-five per cent of ureteral neoplasms are carcinoma while 21 per cent are classified as benign papillomas. This is questioned, as many pathologists consider all urinary tract papillomas as papillary carcinoma Grade 1. The remaining 4 per cent constitute the rare group of sarcomas, hemangiomas or fibromas.

Renner[6] uncovered only 3 cases of primary ureteral neoplasm in 13,000 necropsies at the Vienna Pathological Institute. Two cases were found in 1934 at Johns Hopkins Hospital in 22,000 urologic admissions. At Bellevue Hospital between 1904–1935, only 1 case was reported in 22,810 autopsies, and at the Chicago Cook County Hospital between 1930–1951, only 4 cases were reported in 26,400 necropsies.

Before discussing our cases, we would like to review briefly the pathogenesis and symptomatology of ureteral carcinoma.

The etiology of ureteral epithelial tumors is unknown, but it is closely related to that of renal and vesical epithelial tumors. All theories pertaining to the genesis of carcinoma in other systems also apply here. They occur primarily in males (66 per cent) between the fourth to seventh decades with 75 per cent occurring in the lower third of the ureter.

The most frequent findings and symptoms are hematuria, pain, a palpable mass in the renal area and a mass defect visualized on the pyelogram.[10] Hematuria is present in approximately 75 per cent of cases, a palpable mass (hydronephrotic kidney) in 40 per cent and pain, secondary to distention of the ureter, in approximately 50 per cent of cases. In most of the reported series of cases, the correct preoperative diagnosis was made in approximately 50 per cent.[8] We feel that with an awareness of the clinical picture and proper utilization of intravenous and retrograde pyelography, the diagnostic accuracy can be markedly improved.

We have mentioned two diagnostic aids; namely, the importance of visualizing the entire ureter since smaller lesions which are nonobstructing will present a normal sized ureter and kidney as in 4 of our cases, and the coiling of the catheter at the site of the lesion (Fig. 1*A*). To our knowledge, this latter finding has never been previously described. We explain its mechanism as follows:

In the case of mechanical obstruction of the ureter, such as occurs by a calculus, the ureter below the site of the obstruction would tend to collapse (Fig. 1*B*). Following obstruction by an expanding intraluminal tumor mass, such as a primary ureteral carcinoma, the lumen of the ureter directly above and below the lesion will gradually expand due to tumor growth. Upon passing a retrograde catheter, we have observed that the size of the lumen directly below the tumor is increased sufficiently so that when the catheter is impeded by the tumor mass, it tends to coil within the lumen, and will either remain at this site or, after coiling, pass above the tumor mass. This characteristic coiling occurred in approximately half of our cases and has been of considerable aid in suggesting the presence of an expanding lesion of the ureter.

REPORT OF CASES

CASE I. A fifty-seven year old female (the only female in our series) had gross hematuria several times over a period of one year. Her original work-up was for hemorrhagic cystitis and retrograde pyelography was reported as normal. A subsequent intravenous pyelogram, one year later, was "normal" except that the lower half of both ureters did not visualize (Fig. 2). A retrograde pyelogram at this time (Fig. 3) revealed a defect in the middle third of the right ureter with an essentially normal upper tract. The lesion proved to be a papillary carcinoma (Fig. 4).

CASE II. A seventy-one year old male was admitted with hematuria and symptoms of sepsis one month previously. Intravenous pyelogra-

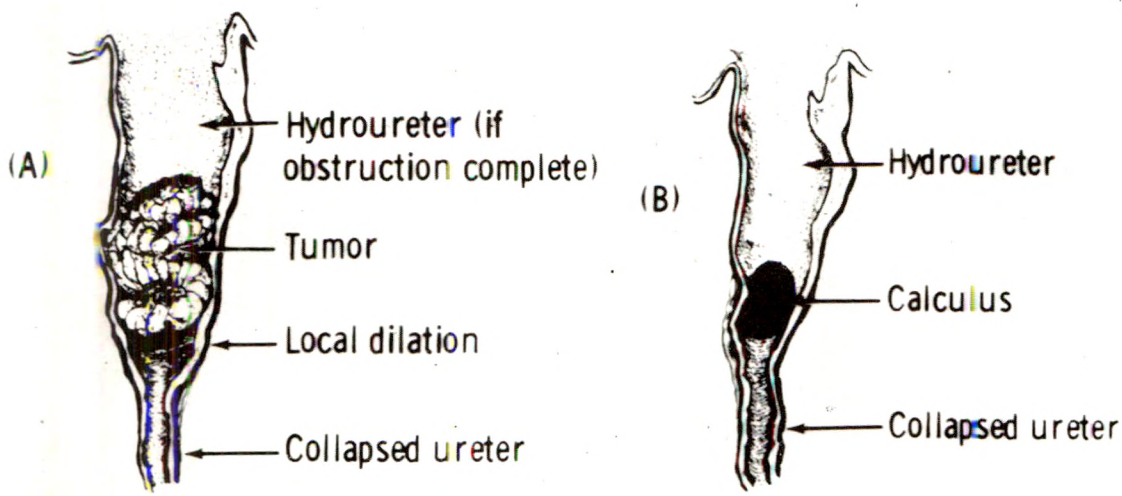


Fig. 1. Case 1. (*A*) Localized dilatation of the ureter below the tumor allowing space for catheter coiling. (*B*) Collapsed ureter below calculus.

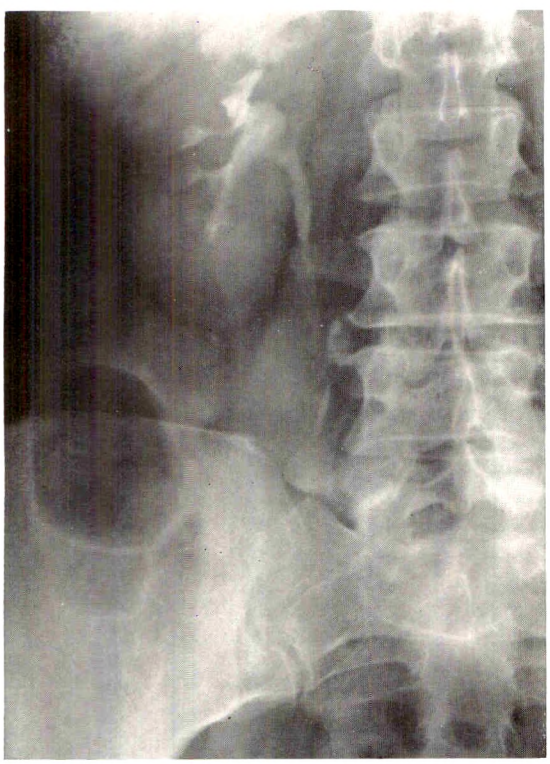


Fig. 2. Case 1. Essentially normal intravenous urogram, but the lower half of the ureter is not visualized. Note the absence of hydronephrosis and hydroureter.

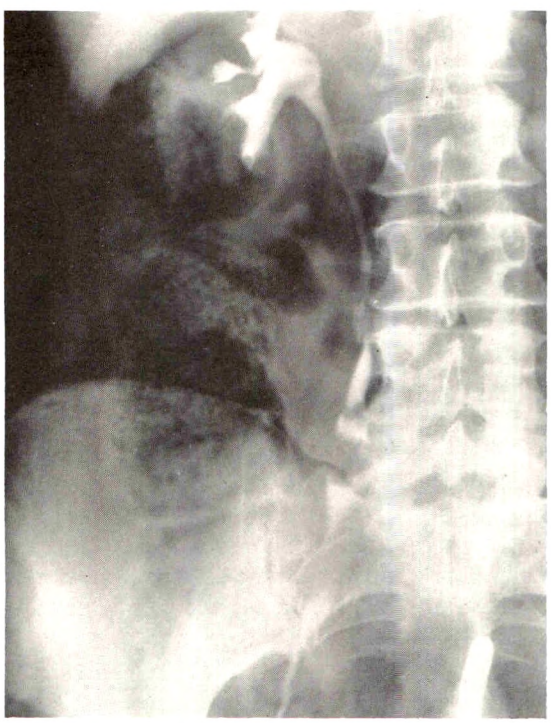


Fig. 3. Case 1. Retrograde urogram revealing filling defect in the middle third of the right ureter. Again note the absence of dilatation above the lesion.

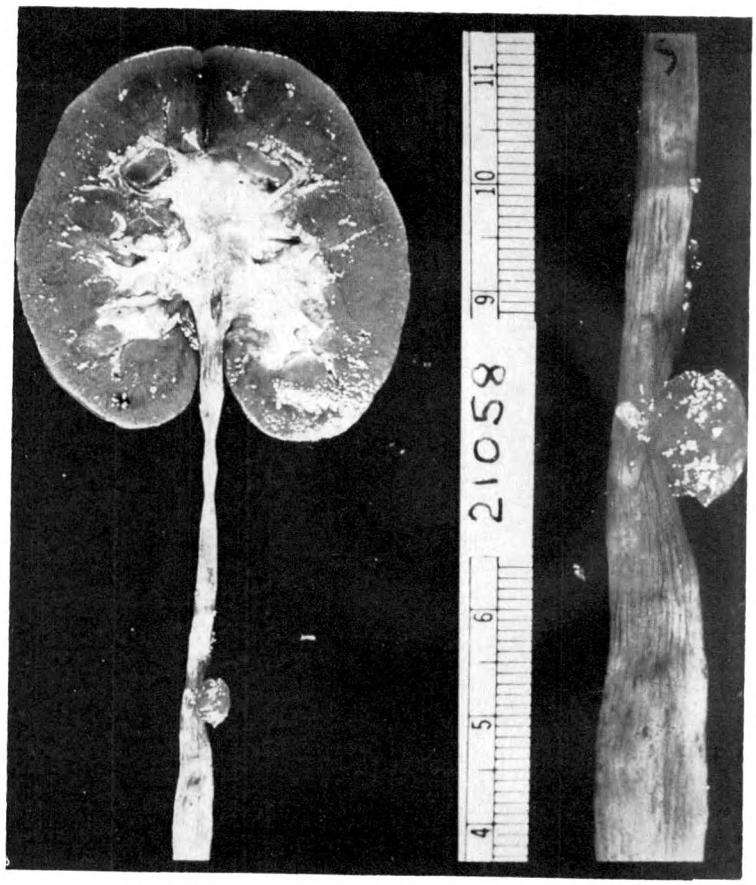


Fig. 4. Case I. Surgical specimen of the papillary carcinoma in the middle third of the ureter. Note the completely normal kidney and ureter above the tumor.

phy revealed a poorly functioning left hydronephrotic kidney. Retrograde pyelograms disclosed the typical coiling of the catheter at the site of the lesion (Fig. 5 and Fig. 6). At surgery an intraluminal papillary carcinoma with associated marked hydroureter and hydronephrosis was found (Fig. 7).

Case III. A fifty-three year old male was admitted because of gross painless hematuria. Intravenous pyelography revealed no function on the left side. The right side was normal. A cystoscopy disclosed a lesion at the ureterovesical junction preventing retrograde pyelography of this side. At surgery a large papillary carcinoma with associated hydroureter and hydronephrosis was found (Fig. 8).

Case IV. A sixty-three year old male presented himself with a three week history of right lower abdominal colicky pain and gross hematuria. Retrograde pyelograms demonstrated the typical coiling effect (Fig. 9). There was hydroureter and hydronephrosis above this. At surgery the lesion was found to be a large fungating intraluminal papillary adenocarcinoma of the lower third of the ureter with marked hydroureter in the segment proximal to the lesion (Fig. 10).

Case V. A sixty-three year old male presented a three day history of hematuria and mild pain on the left side of the abdomen. An intravenous pyelogram appeared essentially normal, but the lower third of the left ureter did not visualize. Retrograde pyelograms revealed the typical coiling of the catheter (Fig. 11); the upper tract appeared normal (Fig. 12). Surgery revealed a lesion which had caused slight dilatation of the ureter, just above the tumor, but the rest of the ureter and kidney was normal. On histopathologic study this proved to be a papillary carcinoma (Fig. 13). Four and one-half years after the original ureteral surgery, the patient returned and examination showed a solitary superficial bladder metastasis.

Case vi. A forty-eight year old male was admitted with right flank pain and hematuria of two months' duration. The upper urinary tracts were essentially normal on intravenous pyelograms. A small cupping defect was noted in the mid-portion of the right ureter on one roentgenogram (Fig. 14).

A retrograde pyelogram revealed large filling defects of the lower third of the right ureter with an essentially normal ureter and kidney above the lesion (Fig. 15). On histopathologic examination a papillary carcinoma was found (Fig. 16).

Case vii. A fifty-nine year old male presented gross painless hematuria of several days' duration. An intravenous pyelogram was reported as normal (Fig. 17) but the lower ureter was not visualized. Cystoscopy revealed a papillary carcinoma of the lower ureter, protruding from the orifice.

PATHOLOGY

Primary tumors of the ureter can be subdivided into two main groups; namely, (A) epithelial and (B) mesodermal. These can be further subdivided into (1) malignant and (2) benign.

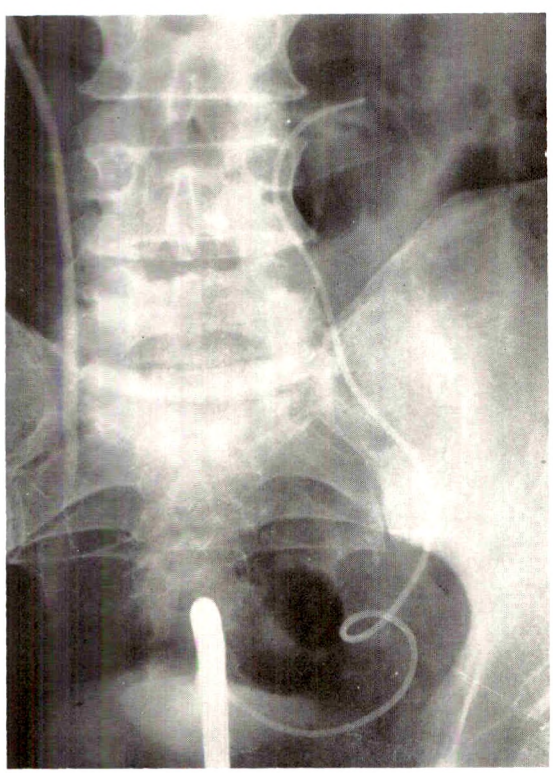


Fig. 5. Case ii. Catheter exhibits typical coiling at the site of the tumor.

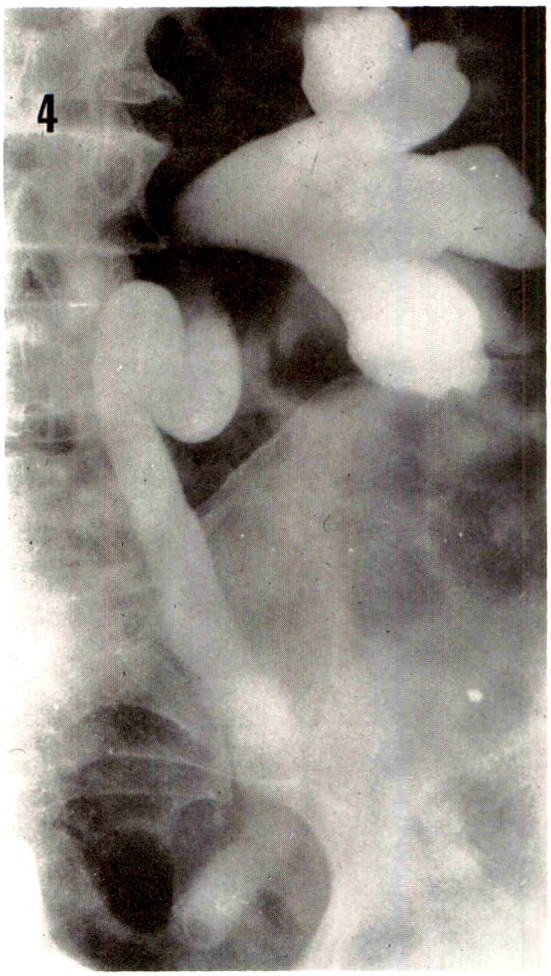


Fig. 6. Case ii. Marked hydroureter and hydronephrosis above the lesion are visualized. The tumor causes a filling defect at the pelvic segment of the left ureter.

A.(1) Primary malignant epithelial tumors are classified as (a) papillary carcinoma of low grade malignancy, (b) papillary carcinoma of high grade malignancy, and (c) infiltrating type. These tumors are usually unilateral, with approximately two thirds occurring in the lower third of the ureter. They metastasize more rapidly than other similar bladder tumors because of the greater lymphatic supply of the ureter and the thinness of the ureteral wall, allowing for quicker permeation. The usual sites of metastases in order of frequency are regional lymph nodes, liver, lumbar verte-

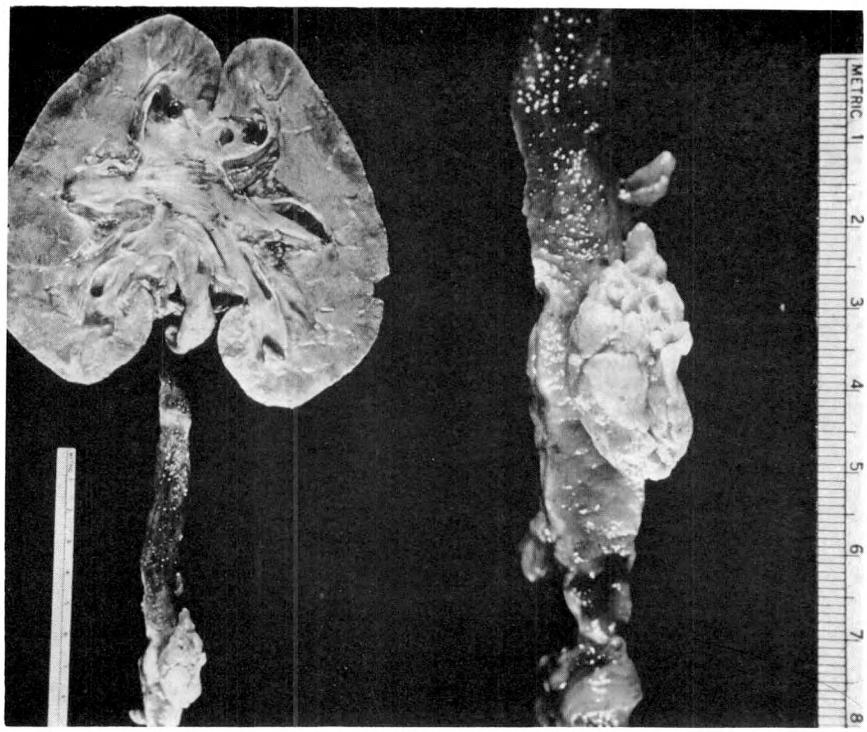


Fig. 7. Case II. Surgical specimen of the papillary carcinoma with marked hydroureter and hydronephrosis.

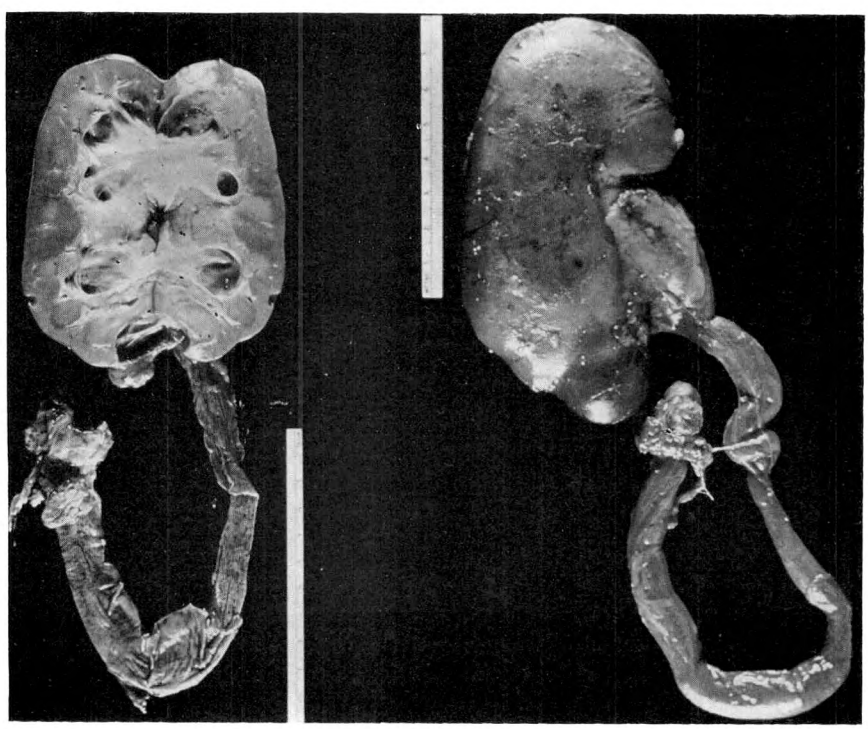
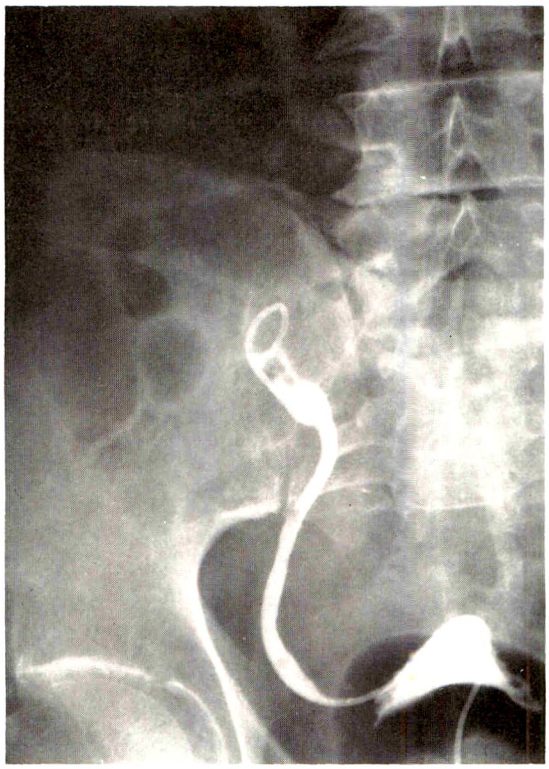


Fig. 8. Case III. Surgical specimen of the large papillary carcinoma at the lower end of the left ureter with associated hydronephrosis and hydroureter.

Fig. 9. Case IV. Coiling of the ureteral catheter with localized dilatation of the ureter at the site of the lesion, and a filling defect and cupping are visualized.



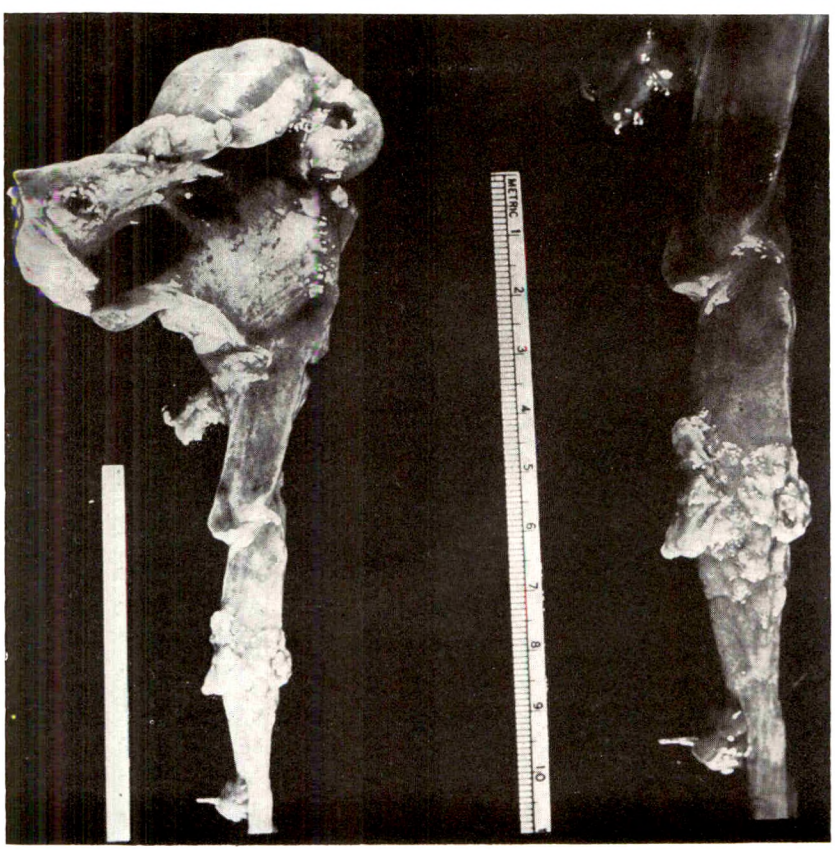
brae, lungs, kidney and adrenal glands.

A.(2) The true benign tumors of the ureter consist of polyps, of which 72 cases have been reported in the literature.[8] The so-called benign papillomas are classified by many pathologists as malignant lesions.

B.(1) Primary malignant tumors of mesodermal origin include the sarcomas which are exceedingly rare and have a very grave prognosis.

B.(2) Benign mesodermal tumors such as fibromas and endometriosis of the ureter are extremely rare.

Fig. 10. (below) Case IV. Surgical specimen of the papillary adenocarcinoma showing dilatation proximal to the lesion.



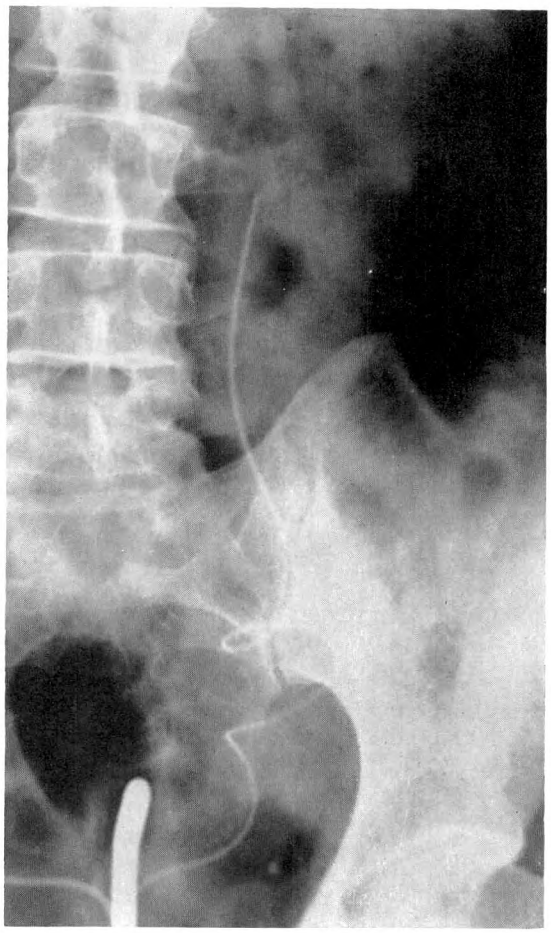


FIG. 11. Case v. Retrograde pyelogram showing the typical coiling of the catheter at the site of the lesion.

PROGNOSIS

Because of the small number of cases and inadequate follow-up, a true evaluation is difficult. It is generally accepted that any patient living more than four years has a favorable prognosis.[8] In our series, one case is alive nine years and several are approaching five years. Only one is dead.

TREATMENT

The best treatment has proved to be radical surgery. Radiation therapy has not been effective either in the primary or metastatic lesion.

The type of surgery performed depends on the patient's general condition, extent and location of the tumor, the presence or absence of metastases and the condition of the opposite kidney. A total nephro-ureterectomy and a partial cystectomy is the usual preferred treatment. When radical surgery is not indicated or cannot be performed, other types of surgery which can be helpful are simple nephro-ureterectomy, resection of the tumor with end to end anastomosis and local reimplantation

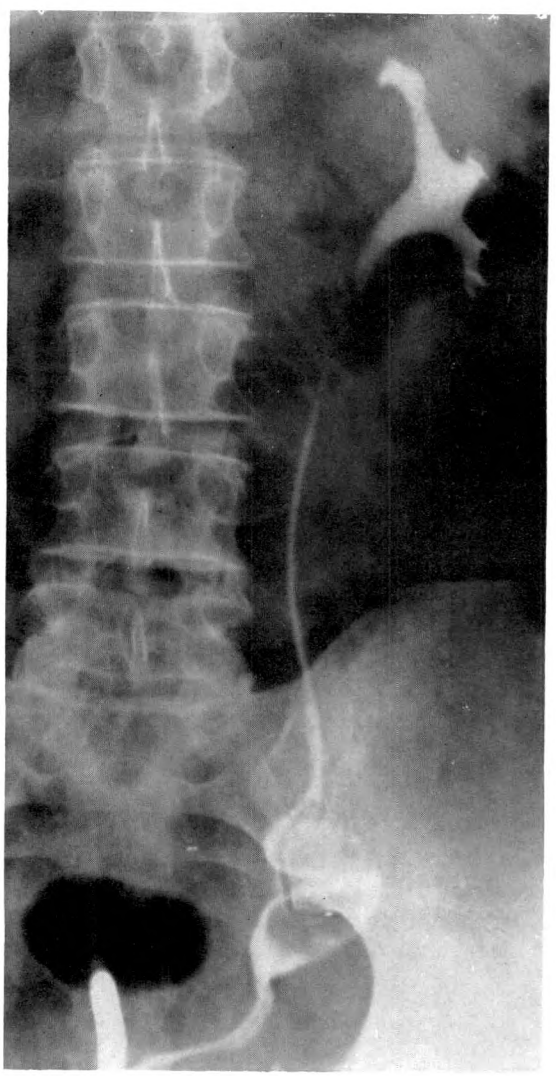


FIG. 12. Case v. Retrograde study revealing a normal ureter and kidney without dilatation above the lesion. A filling defect and localized dilatation in the ureter at the site of catheter coiling are also visualized.



FIG. 13. Case v. Surgical specimen of the papillary carcinoma of the lower third of the left ureter.



FIG. 14. Case vi. Intravenous urogram showing no evidence of hydroureter and hydronephrosis. Cupping of the margins of the ureter at the site of the lesion at the level of L-5 is visualized.

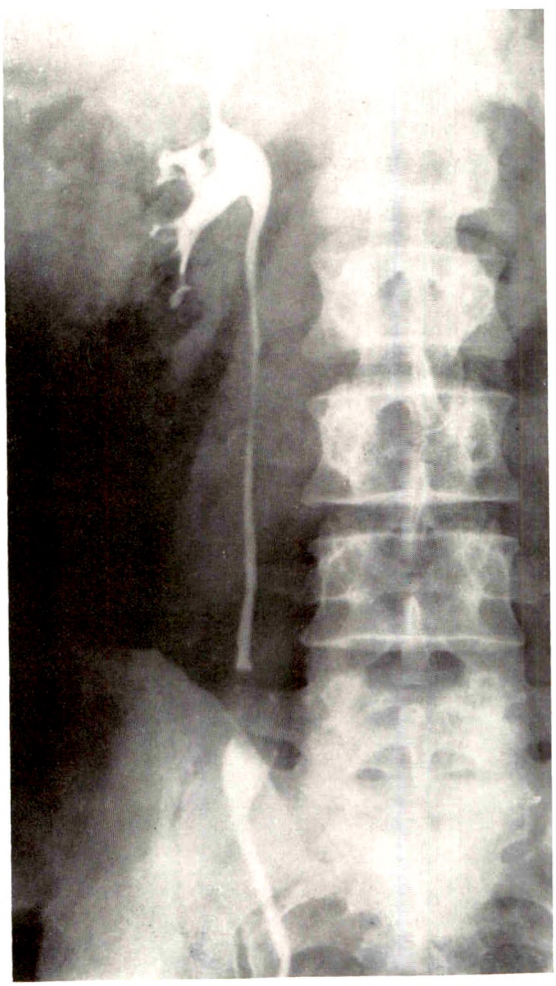


FIG. 15. Case vi. Retrograde study showing a filling defect and cupping of the ureter at the site of the tumor. Note again the lack of dilatation above the lesion.

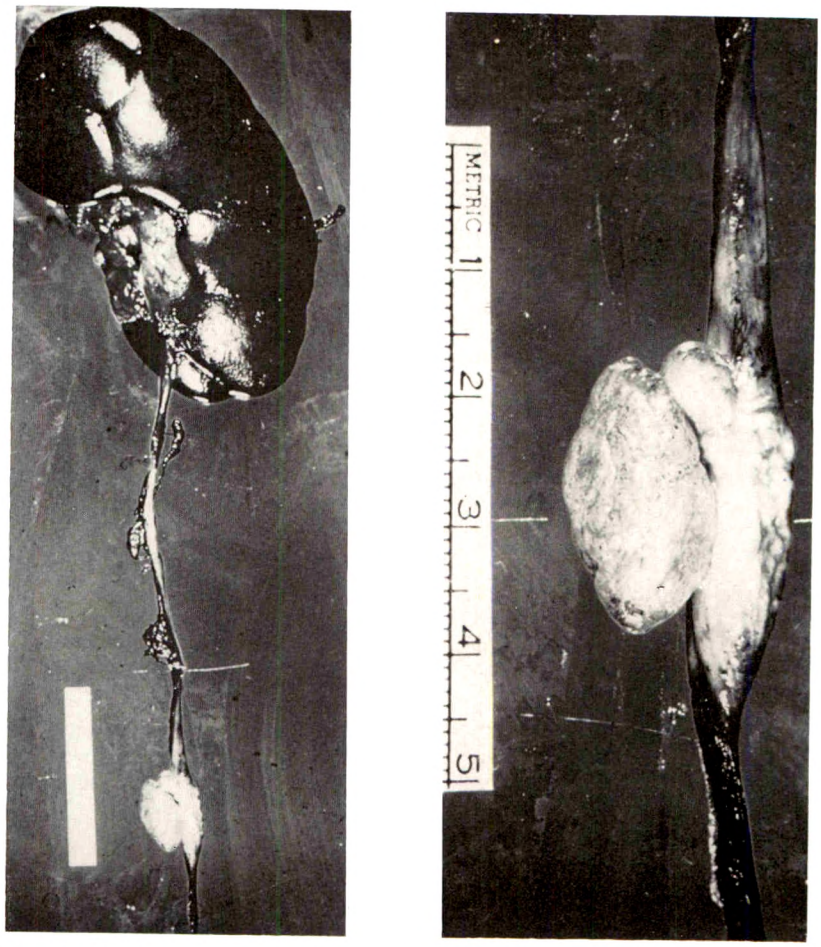


Fig. 16. Case VI. Surgical specimens of the papillary carcinoma and normal kidney and ureter.

of the ureter into the bladder or renal pelvis.

Secondary ureteral tumors involve the ureter by direct extension from neighboring organs, occasionally by metastatic emboli from distant organs and by metastatic implants via the urinary route from the kidney or bladder.

SUMMARY

1. The classic clinical and roentgenologic findings of primary carcinoma of the ureter, stressing two signs which we have found of value in early diagnosis, are presented.

2. The diagnostic triad most often emphasized by all authors consists of gross hematuria, often painless, occurring in the fourth through seventh decades of life; hydronephrosis or nonfunctioning kidney revealed by intravenous pyelography; and a mass lesion in the ureter constituting a filling defect with marginal cupping at the lower and upper ends of the lesion.

3. In analyzing our 7 cases, we have been impressed by the number of normal appearing intravenous pyelograms. This stresses the importance of adequate and complete visualization of the entire ureter in every case of gross hematuria. Nonvisualized segments of the ureter attributed to peristaltic waves must therefore be re-evaluated in the light of our findings. Retrograde pyelography is often required. Hydronephrosis and nonfunctioning kidneys are manifestations of the disease at a later stage when the lesion has progressed to such an extent as to cause partial or complete obstruction.

4. Coiling of the ureteral catheter just



Fig. 17. Case VII. Intravenous urogram with essentially normal findings except for nonvisualization of the lower two inches of the ureter just proximal to the ureterovesical junction.

below the lesion occurs on a mechanical basis, and, when present, is highly suggestive of an expanding intraluminal mass, usually carcinoma. This diagnosis can be suggested even before the instillation of contrast medium.

5. These findings are emphasized in the hope that primary carcinoma of the ureter will be considered in every case of hematuria, and that earlier diagnosis will therefore be made.

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VENA CAVAGRAPHY IN THE MANAGEMENT OF MALIGNANCY*

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THE extent and location of malignant disease are two of the most important factors influencing the choice between curative and palliative therapy. Visualization of the superior and inferior venae cavae can show pathology in the mediastinum and the retroperitoneal space that is missed by the more commonly employed roentgenographic procedures. These great veins, which are readily deformed by adjacent pathology, are easily and safely visualized with contrast material. A simplified technique of vena cavagraphy will be illustrated and representative cases presented from over 400 studies.

Cavagrams are of particular value in cases of lymphoma, where the clinical staging is of the utmost importance in determining initial and subsequent therapy.[1,2] Accurate staging is not possible without adequate evaluation of the mediastinal and retroperitoneal lymph nodes. Occult malignancies in the retroperitoneal area, suspected clinically, can often be revealed by inferior vena cavagraphy because of the large number of lymphatic nodes surrounding this great vein. Pathologic enlargement of the right adrenal gland, right kidney, liver, and head of the pancreas can be detected by this technique. Evaluation of therapeutic results in retroperitoneal disease and determination of the need for further therapy are greatly aided by this objective method of evaluation.

ANATOMIC CONSIDERATIONS

Although only fifteen per cent of the retroperitoneal space is occupied by the inferior vena cava, the majority of the retroperitoneal lymph nodes are concentrated along the course of this great vessel. The right adrenal gland, right kidney, liver and head of the pancreas are in intimate contact with it (Fig. 1). The thin wall and low hydrostatic pressure of the inferior vena cava permit this structure to be easily deformed, displaced or obstructed by adjacent masses. Normal inferior vena cavagrams are illustrated in Figure 2. Of sig-

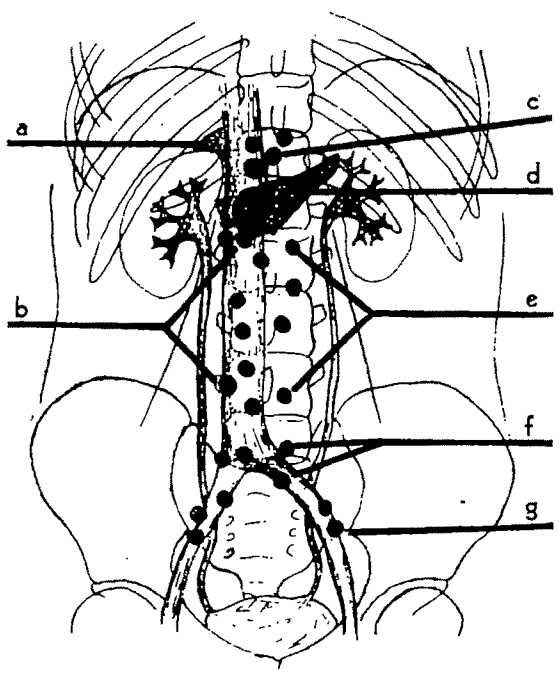


FIG. 1. Schematic diagram of the major relationships of the inferior vena cava. The right lateral aortic lymph nodes surround the vena cava. (a) Right suprarenal gland; (b) right lateral aortic lymph nodes; (c) main mesenteric lymph nodes; (d) pancreas; (e) left lateral aortic lymph nodes; (f) subaortic and common iliac lymph nodes; (g) external iliac lymph nodes.

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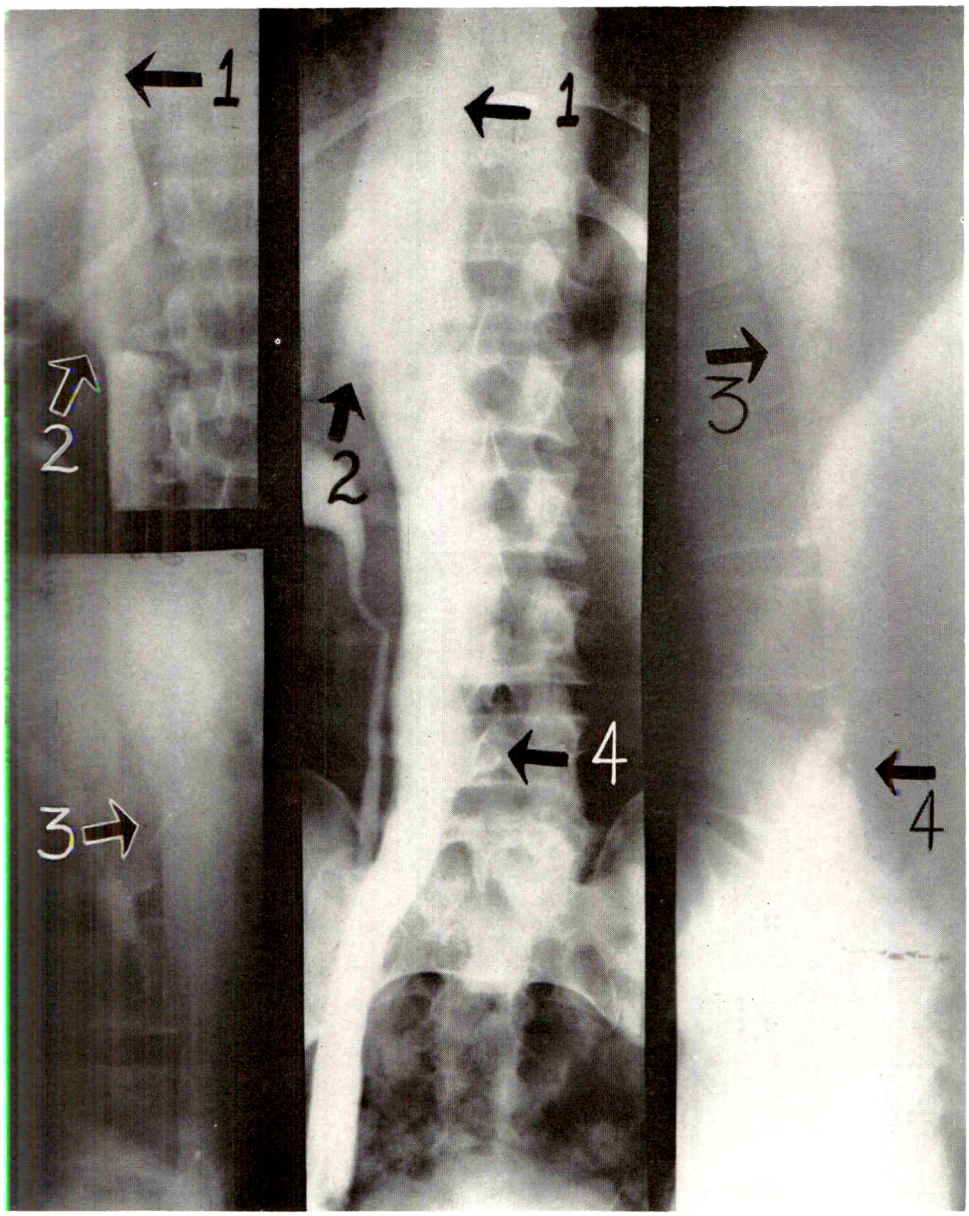


Fig. 2. Normal inferior vena cavagrams. (1) Variation in the course of the vena cava as it lies in the fossa venae cavae on the posterior surface of the liver. This may be a shallow groove or may be a canal covered by a thin portion of the hepatic substance. (2) Change in width of the vena cava and the irregularity in the contrast column at the insertion of the right and, to a lesser extent, the left renal vein. (3) Smooth pressure defect produced by the right renal artery as it courses posterior to the vena cava near the L2 level. (4) Normal defect due to compression by the right common iliac artery.

nificance is the widening, dilution and apparent irregularity of the column of contrast material at the level of the renal veins. At the origin of the inferior vena cava, compression by the right common iliac artery normally produces a defect which should not be interpreted as pathologic. The influx of blood from the ipsilateral internal iliac vein and the contralateral common iliac vein may also produce an

TABLE I

NORMAL MEASUREMENTS OF THE INFERIOR VENA CAVA*

Level		L4	L3	L2	L1	D12	D11
Distance from the posterior border of the inferior vena cava to the anterior border of the vertebral body (lateral view)	Average	−2.6	−1.2	3.0	4.0	3.6	14.8
	Range	−11–0	−8–2	−6–11	−5–16	−2–10	0–35
Distance from the lateral margin of the inferior vena cava to the middle of the vertebral body (anteroposterior view)	Average	35.2	36.3	38.8	44.4	42.2	42.4
	Range	25–41	25–45	25–46	27–55	28–55	25–54
Diameter of the inferior vena cava (lateral view)	Average	18	20	20	23	25	28
	Range	10–29	14–30	19–30	14–32	19–34	20–35
Diameter of the inferior vena cava (anteroposterior view)	Average	28.4	28.5	29.0	33.2	31.0	26.4
	Range	24–33	24–36	25–37	26–45	24–43	18–37

* All measurements are in millimeters. Negative values refer to the millimeters of overlap of the vena cava on the vertebral body.

irregularity in the contrast column. The right renal artery indents the posterior aspect of the inferior vena cava as it courses to the kidney. The caudate lobe of the liver indents the left margin of the vena cava at the D11–D12 level. The normal measurements of the vena cava at its various levels are given in Table I.

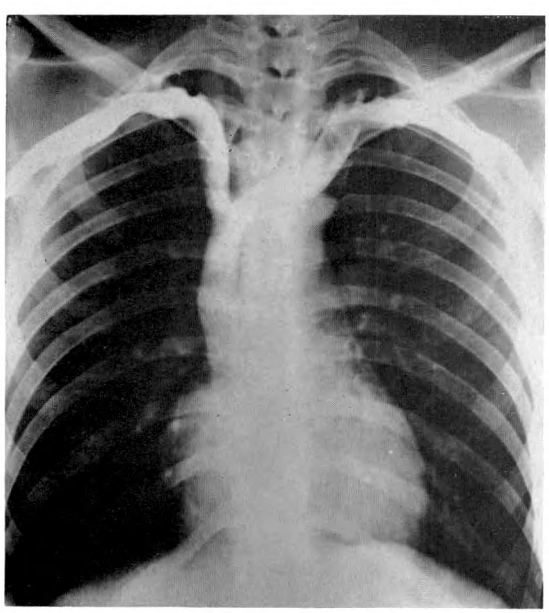


FIG. 3. Normal superior vena cavagram with the major tributaries. The advisability of utilizing the left antecubital vein is illustrated by the course of the left innominate vein across the mediastinum. This bilateral injection was done for illustration.

The superior vena cava and the innominate veins are intimately related to most of the lymph nodes and other structures of the superior mediastinum. The left innominate vein traverses the entire width of the superior mediastinum; therefore, visualization of the superior vena cava via its tributaries on the left is more informative than right sided injection (Fig. 3; 13, *A* and *B;* and 14, *A*, *B* and *C*).

TECHNIQUE

The technique of superior and inferior vena cavagraphy differs from intravenous pyelography primarily in the site and speed of injection and timing of the film exposures. Superior vena cavagraphy is a simple procedure performed by the rapid injection of 30 cc. of 50 per cent hypaque into a left medial antecubital vein, with the patient supine. A No. 18 gauge needle is utilized and while the patient takes a deep, slow breath the injection is completed within five seconds. This can be a unilateral or bilateral injection. The first film of the chest is exposed at the end of injection. A second film is exposed six seconds later to evaluate obstruction and collateral circulation.

A simplified technique of inferior vena

cavagraphy has been described in previous publications.[5,6] The technique consists essentially of the rapid injection of contrast material into the right femoral vein with the left femoral vein occluded and the head of the table elevated ten degrees. The injection is made during the expiratory phase of respiration. A No. 17 gauge needle is utilized. It is advisable that a bevel no sharper than 45 degrees be used to facilitate threading of the needle and to minimize the possibility of extravasation. Films of the abdomen are exposed in both anteroposterior and lateral projections. Following these injections pyelograms are taken. Figure 4 illustrates the simplicity of the technique.

CLINICAL APPLICATION

In the past four years over 400 vena cavagrams have been performed at the U. S. Naval Hospitals, Pensacola, Florida, and St. Albans, New York, to aid in the management of patients with malignant disease of various types. These studies are of particular value in cases of lymphoma where the clinical staging of the disease is of utmost importance in determining initial therapy. Accurate clinical staging of lymphoma is not possible without adequate evaluation of the mediastinal and retroperitoneal lymph nodes. When inferior vena cavagraphy demonstrates retroperitoneal lymphadenopathy, intensive therapy to the mediastinal and/or peripheral lymph nodes would needlessly deplete the patient's gen-

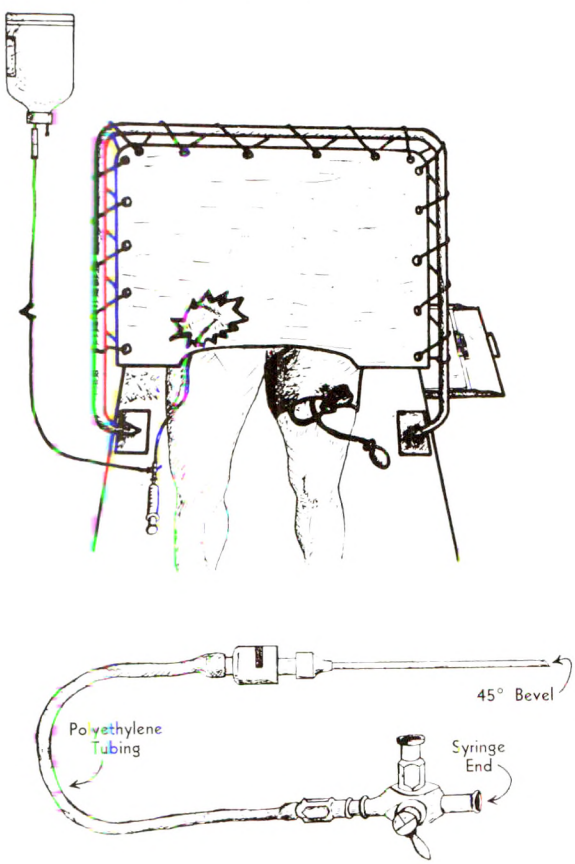


Fig. 4. Diagram of the technique of inferior vena cavagraphy. The sphygmomanometer is inflated to decrease the dilution of the contrast material by blood from the contralateral lower extremity.

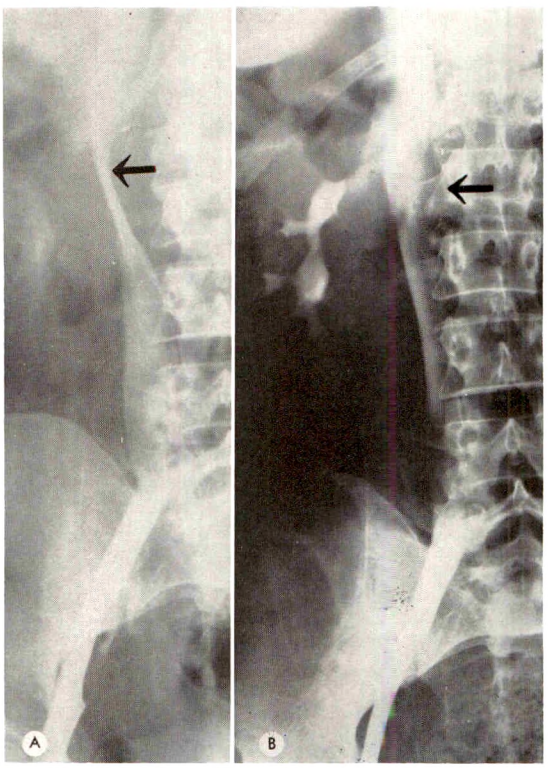


Fig. 5. (*A*) The inferior vena cavagram illustrates a sharply localized, large, extrinsic pressure defect at the D12 to L3 level. The intravenous pyelogram was normal. (*B*) After a 3,400 r tumor dose to this well-defined retroperitoneal region, the inferior vena cavagram was normal and remained so for the following year. Adequate radiation therapy was thus delivered to a smaller portal; irradiation of a larger field or the use of chemotherapy was unnecessary. Either one of these techniques would have depleted the body economy needlessly.

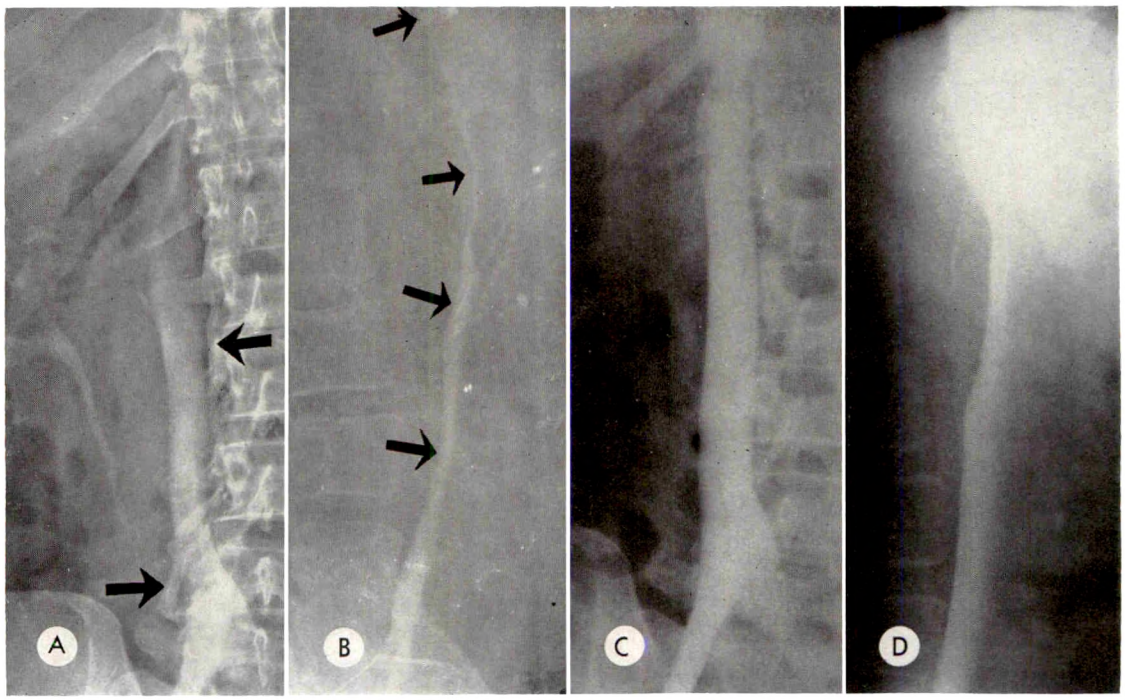


FIG. 6. (*A* and *B*) Massive lymphadenopathy posterior to and surrounding the inferior vena cava is well illustrated in the lateral projection. In the anteroposterior projection the high grade obstruction at the L1–L2 level is evidenced by the filling of the right ascending lumbar vein (upper arrow in *A*) and its tributaries (lower arrow in *A*). Deviation of the inferior vena cava is also seen in this projection. In the absence of a Valsalva maneuver, the demonstration of collateral circulation on an inferior vena cavagram is pathognomonic of a complete or incomplete obstruction more cephalad. (*C* and *D*) Inferior vena cavagrams following a 3,500 r tumor dose delivered through opposing fields to the entire abdomen. Note the marked improvement in the configuration of the vena cava, the absence of visualized collaterals, and the need for localized radiation therapy to the L1–L2 level, which was given subsequently.

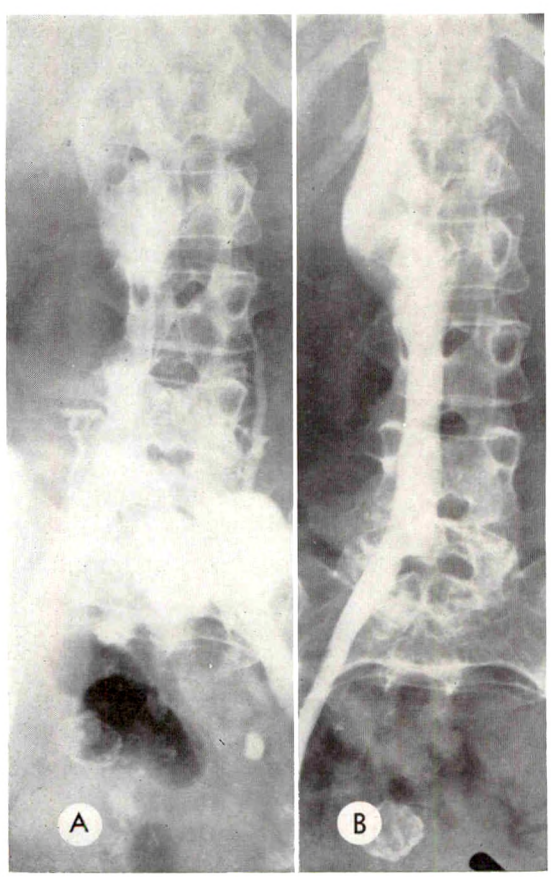


FIG. 7. Giant follicular lymphoma of the left cervical region was diagnosed by biopsy four years before present admission for malaise and weight loss. (*A*) The inferior vena cavagram demonstrates partial obstruction at the L3-L4 level with collaterals consisting of both right and left ascending lumbar veins. Distortion at L1-L2 indicates other lymph node involvement. (*B*) Following a 3,000 r tumor dose to the L1-L5 region in forty-one days, dramatic symptomatic improvement occurred. A calcified uterine fibromyoma is present in the pelvis.

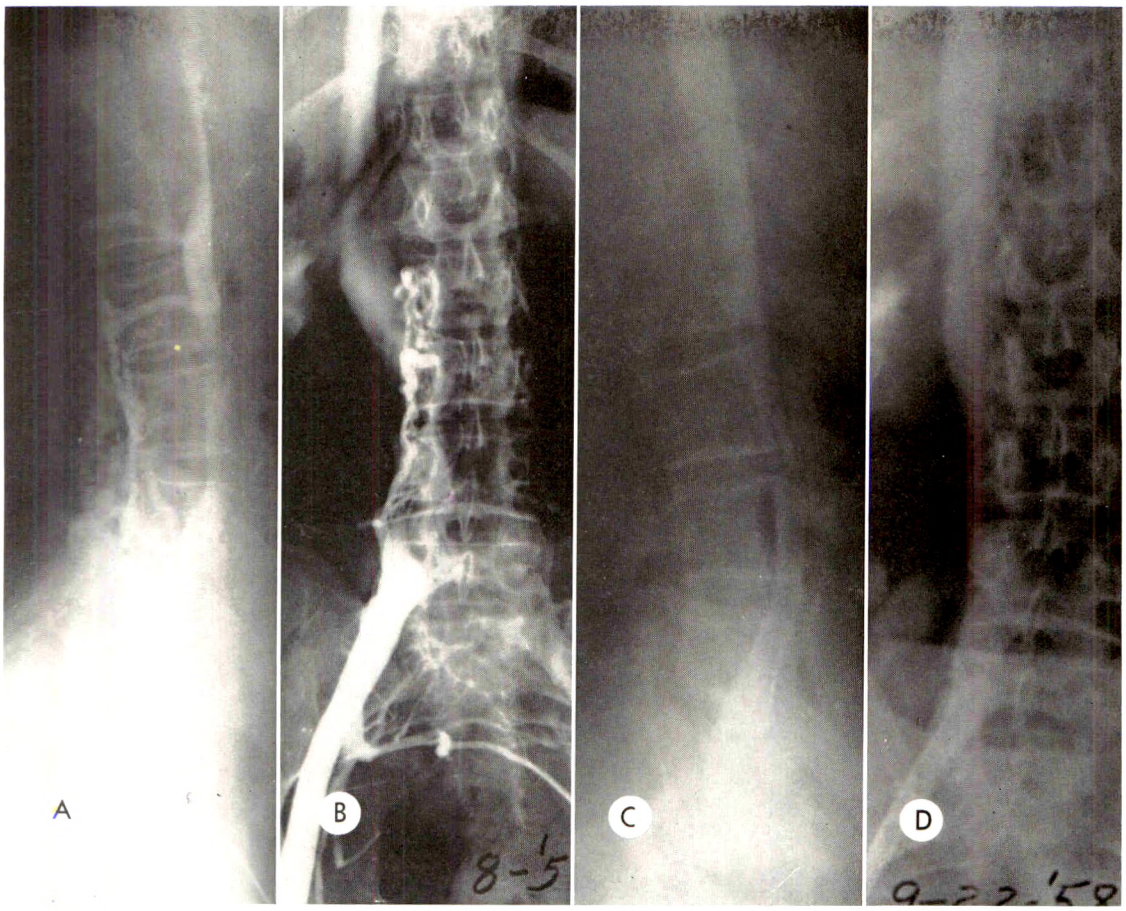


Fig. 8. This fifty-six year old white female received radiation therapy for giant follicular lymphoma of the cervical lymph nodes in 1953. Unexplained weight loss and flank pain were present on admission. Physical examination was negative. (*A* and *B*) Inferior vena cavagrams reveal a partial obstruction of the vena cava overlying L_4 with extensive collateral circulation and a second mass from D_{11} to L_2 elevating and displacing the vena cava. (*C* and *D*) Following a 3,000 r tumor dose to these retroperitoneal lymph nodes the inferior vena cava returned to normal except for slight elevation and displacement at the D_{12} to L_1 level. Note the absence of collateral circulation.

eral economy. In this case a less vigorous plan of therapy may be indicated. On the other hand, when the presence of localized disease is supported by negative vena cavagrams, more intensive radiation therapy is then indicated.

In occult malignancies special studies often fail to reveal the suspected neoplasm. Figure 5, *A* and *B*, illustrates a case of Hodgkin's disease which was undiagnosed for fifteen months, during which time the patient was hospitalized on two separate occasions. Special studies including bone marrow examinations were repeatedly negative. When a lymph node in the axilla became enlarged and was biopsied, the diagnosis of Hodgkin's disease was made. An inferior vena cavagram at that time revealed extensive retroperitoneal involvement which was undoubtedly the cause of intermittent fever and malaise. Had an inferior vena cavagram been done as an integral part of the routine work-up of occult malignancy the diagnosis could have been made several months sooner. After the presence of a retroperitoneal neoplasm is established, serial vena cavagrams provide objective evidence of the response to therapy. Figure 6, *A–D*, illustrates a case in which extensive retroperitoneal lymph-

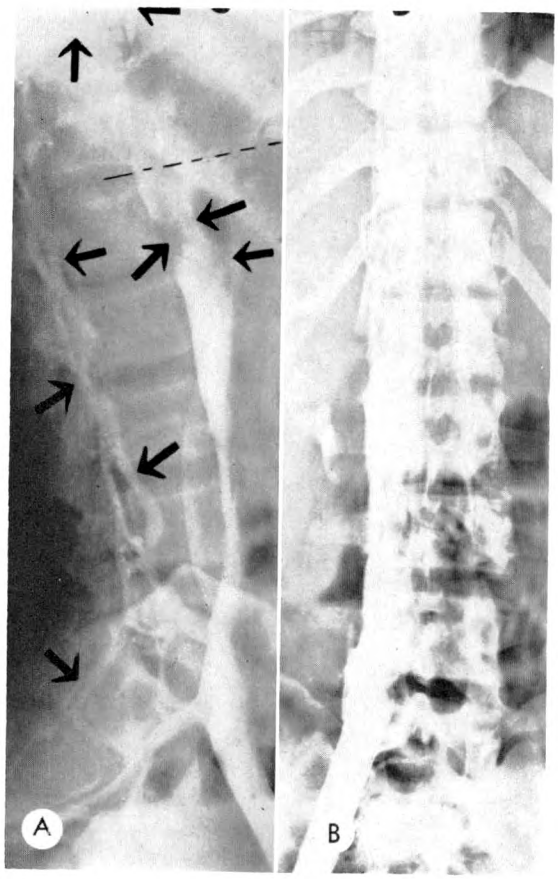


FIG. 9. This twenty-six year old white male was admitted with nausea, vomiting, and progressive pain in the lumbar region for the preceding month. Intravenous pyelography, upper gastrointestinal series and barium enema examination were normal. (*A* and *B*) Inferior vena cavagrams demonstrate numerous masses compressing the vena cava in the lower lumbar region and completely obstructing the flow of contrast material at L_1. Note the large collaterals with the contrast material again entering the vena cava at D_{11}-D_{12}, which is above the complete block. One week later the patient became comatose and expired. Autopsy revealed anaplastic metastatic carcinoma in the brain and the same cell type in the retroperitoneal lymph nodes. The primary site could not be determined. Of interest is the demonstration by vena cavagraphy of the extensive collateral circulation as a possible route for the cerebral metastases.

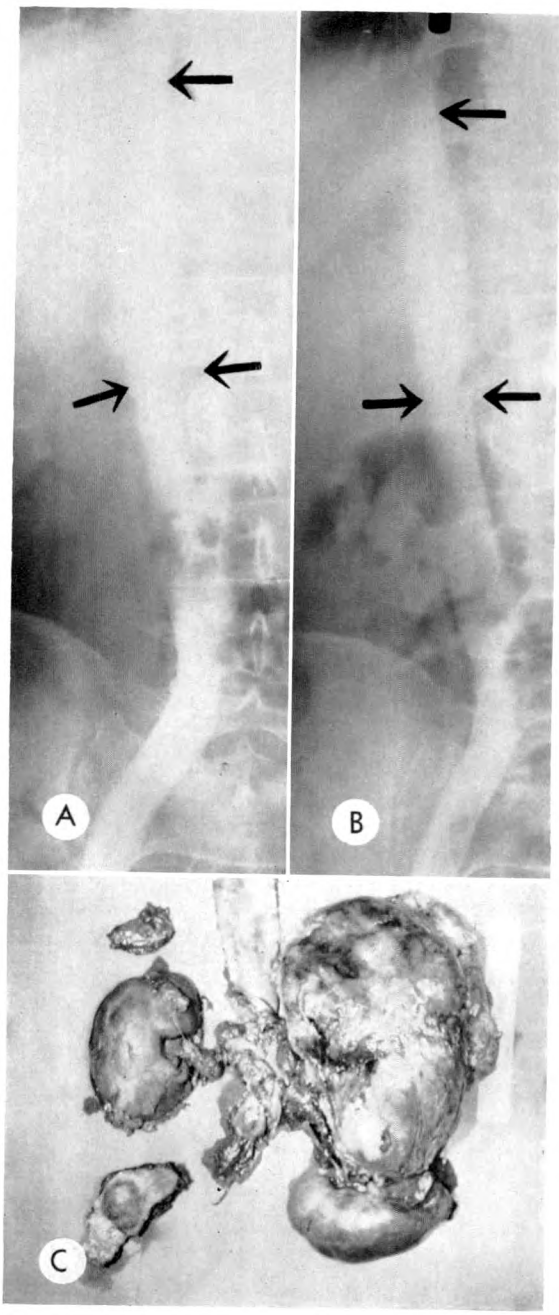


FIG. 10. A thirty-five year old white male was admitted with a large left abdominal mass which displaced and distorted the collecting system of the left kidney. (*A*) The inferior vena cavagram demonstrates a mass of lymph nodes surrounding the vena cava at the L_2-L_3 level and a suggestive mass at D_{11}. Needle biopsy revealed a carcinoma of the adrenal cortex. Because of the metastatic spread disclosed by the inferior vena cavagram,

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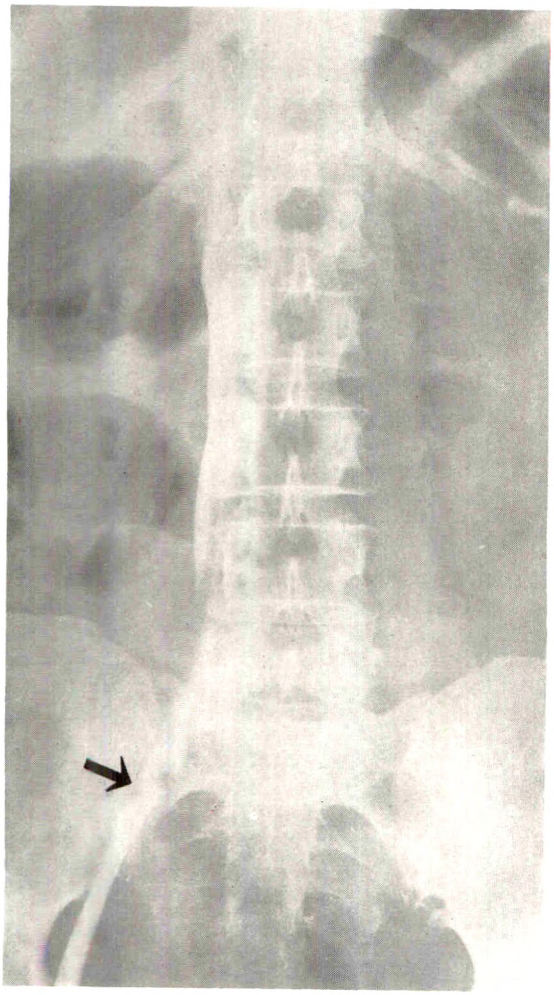


Fig. 11. An inferior vena cavagram demonstrates metastatic right common iliac lymph nodes in a patient with carcinoma of the cervix. Note the filling defect laterally, at a site where there are no tributaries to this vein. Surgery confirmed the roentgenographic findings.

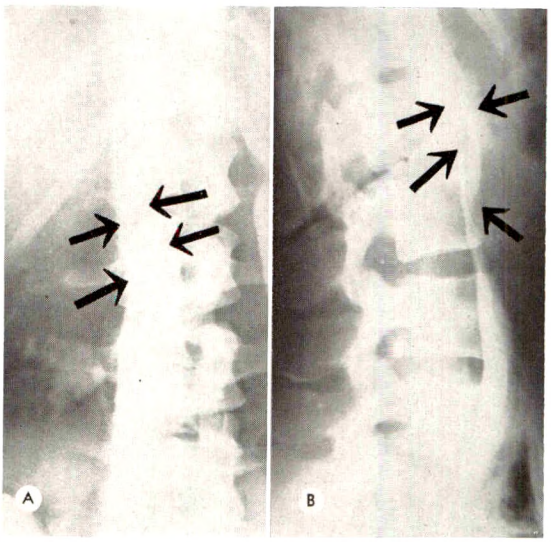


Fig. 12. A forty-three year old white female was admitted with abdominal distention. Pelvic examination revealed a mass in the pelvis. (*A* and *B*) Inferior vena cavagrams reveal a second mass at the L1-L2 level. Note the pressure defects on the anterior surface of the vena cava rather suggesting an abdominal origin. Surgery revealed a carcinoma of the ovary with peritoneal implants and a fixed mass in the region of the celiac axis.

radiation therapy was given to the left flank and to the metastatic L2-L3 region. (*B*) One week after completion of therapy, the inferior vena cavagram shows considerable improvement at the L2-L3 treatment site, but the suspicious D11 area is grossly abnormal. At this time small metastatic nodules began to appear in the lungs. (*C*) At autopsy the diagnosis was confirmed and the metastatic masses at L2 and D11 were found to be separate from the primary adrenal tumor. Note the enormous size of the left adrenal gland as compared to the right adrenal gland and kidneys.

adenopathy was not apparent at exploratory laparotomy because of the massive mesenteric lymph nodes. Biopsy of the mesenteric lymph nodes revealed giant follicular lymphoma. A postoperative inferior vena cavagram revealed marked elevation caused by retroperitoneal lymphadenopathy. Serial inferior vena cavagrams demonstrated the response to therapy (Fig. 6, *C* and *D*).

Partial or complete obstruction of either of the venae cavae can be readily diagnosed and the exact site determined only by vena cavagraphy (Fig. 7–14). This is of primary value in inferior vena caval obstruction, in which clinical symptoms are absent in 50 per cent of cases.[4] Intensive local radiation therapy to these sites may prevent or alleviate distressing obstructive symptoms. Illustrative cases are presented in Figures 7–12.

Although routine methods are usually adequate in evaluating pelvic pathology, the anterolateral areas of the pelvis are

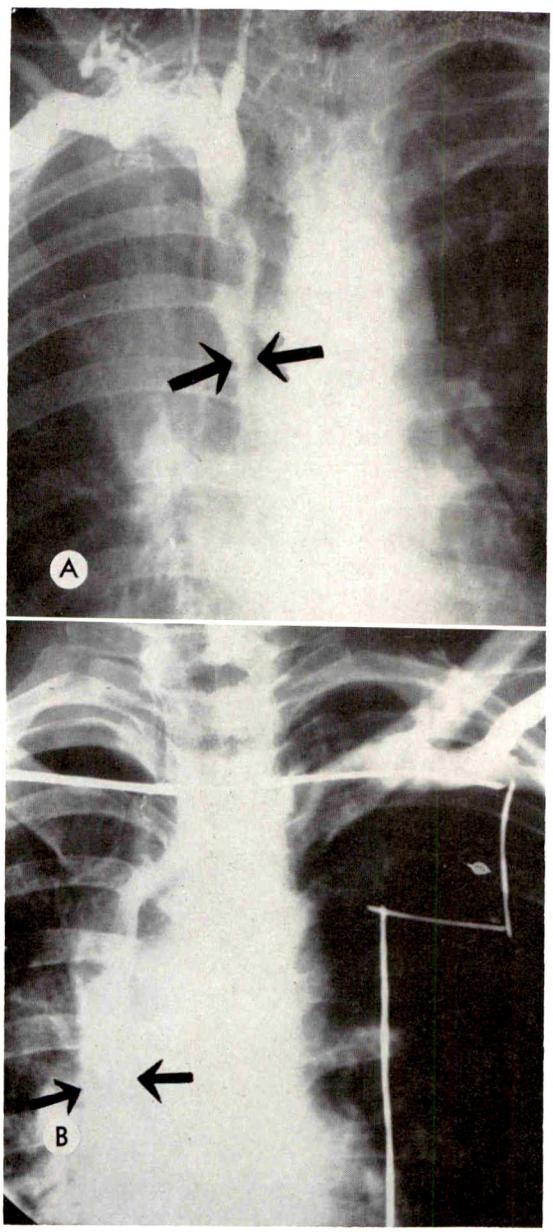


FIG. 13. This fifty year old white female was admitted because of a mass seen on a routine chest roentgenogram five years following a left radical mastectomy for carcinoma. Biopsies of the scalene lymph nodes were negative and open thoracotomy was scheduled. During the induction of anesthesia the patient suddenly developed a superior vena caval obstruction with marked cardiovascular changes. (*A*) A superior vena cavagram taken the following day revealed the almost complete obstruction. Had the study been performed before the anesthesia the near fatal reaction could have been prevented. (*B*) A superior vena cavagram taken after three weeks of radiation therapy demonstrates the normal width of the vena cava. Biopsy of the mass was performed without difficulty under general anesthesia. Microscopic sections revealed carcinoma compatible with breast carcinoma.

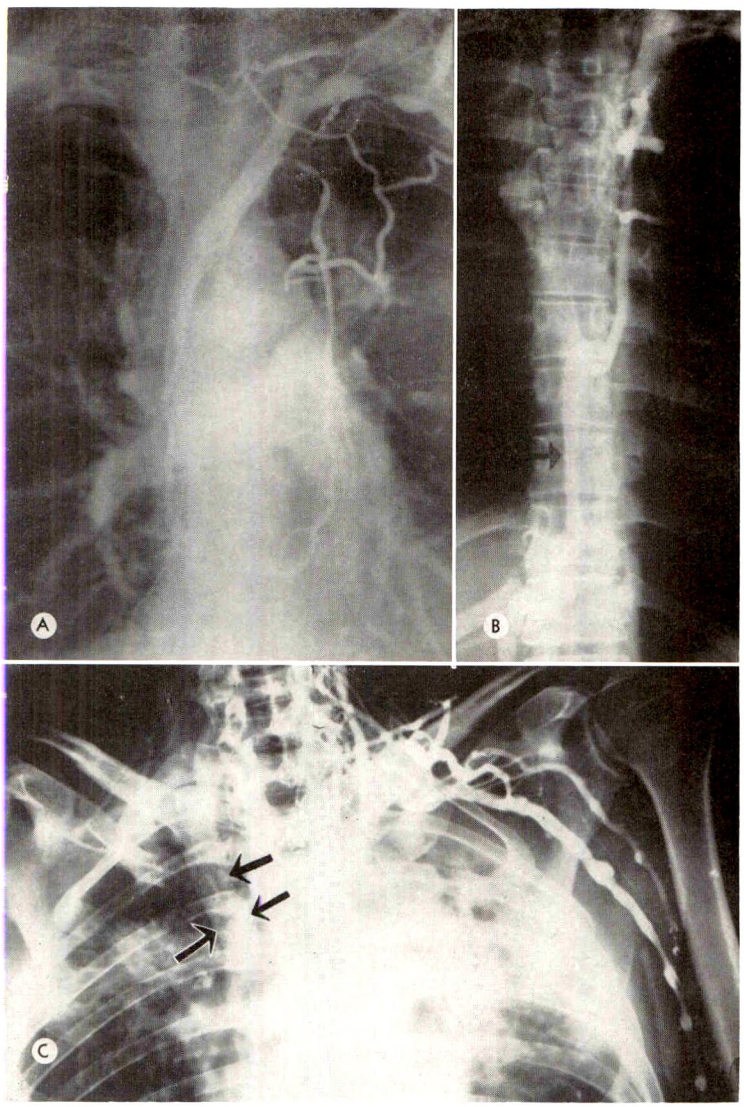


Fig. 14. The mediastinal venous collateral circulation which is visualized varies with the site of the obstruction. (*A*) With incomplete low superior vena caval obstruction the internal mammary veins are well visualized. (*B*) Complete obstruction of the superior vena cava results in visualization of the hemiazygos and azygos systems. (*C*) Complete obstruction of one innominate vein causes the contrast material to reflux through innumerable cervical veins to the contralateral innominate vein.

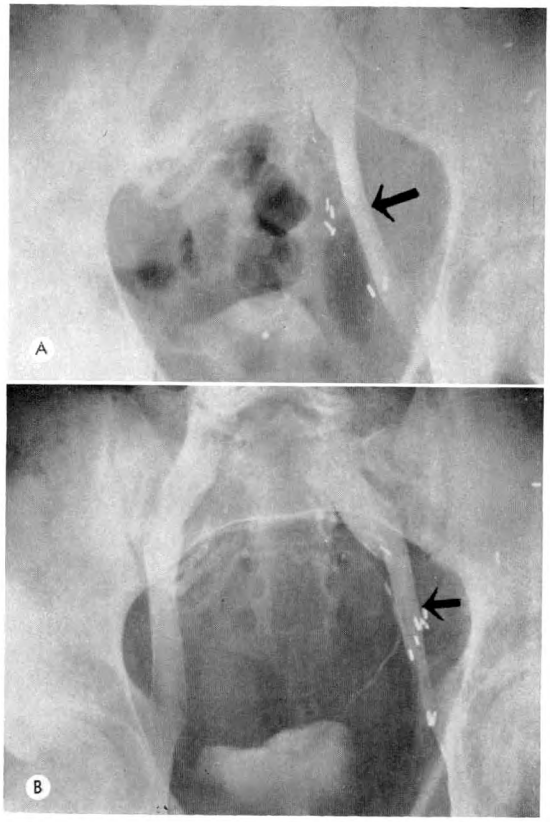


FIG. 15. A palpable mass in the left iliac fossa was biopsied revealing a reticulum cell sarcoma. Before radiation therapy a left femoral injection (*A*) outlines the medial confines of the tumor and provides a basis for evaluating the radiation response. After a 3,500 r tumor dose in three weeks, a repeat injection (*B*) reveals the minimal deformity of the common iliac vein; this has remained unchanged over the past year. A sensitive objective method for detecting possible early recurrence is provided.

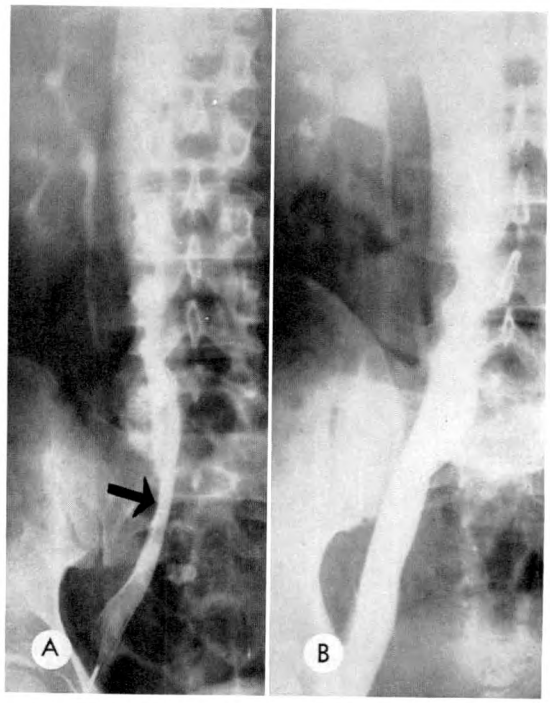


FIG. 16. An obese white male, thirty-eight years of age, was clinically suspected of having a malignant process, but physical examination and routine roentgenographic and laboratory findings were negative. (*A*) An inferior vena cavagram reveals a large mass of iliac lymph nodes (arrow). Compare with *B*, a normal inferior vena cavagram. Biopsy revealed Hodgkin's disease. Following a 3,500 r tumor dose in three weeks to the right lower quadrant, a repeat inferior vena cavagram was negative and has remained so at three, six, and twelve month intervals.

better studied by iliac venography. Examples of pathology demonstrated by contrast visualization of these tributaries of the inferior vena cava are illustrated in Figures 15, *A* and *B;* 16, *A* and *B;* and 17, *A* and *B*.

The inferior vena cava is intimately related to the right adrenal gland, right kidney, liver, and head of the pancreas. Therefore, pathologic enlargement of these structures can be detected by inferior vena cavagraphy.

SUMMARY

Over 300 vena cavagrams have been employed in the evaluation and management of patients with various malignancies in the past four years at the U. S. Naval Hospitals, Pensacola, Florida, and St. Albans, New York. The technique of both superior and inferior vena cavagraphy has been briefly described. Anatomic relationships of the venae cavae have been discussed and illustrative cases of a variety of tumors presented. These studies have been of particular value in cases of lymphoma, and genitourinary and mediastinal tumors.

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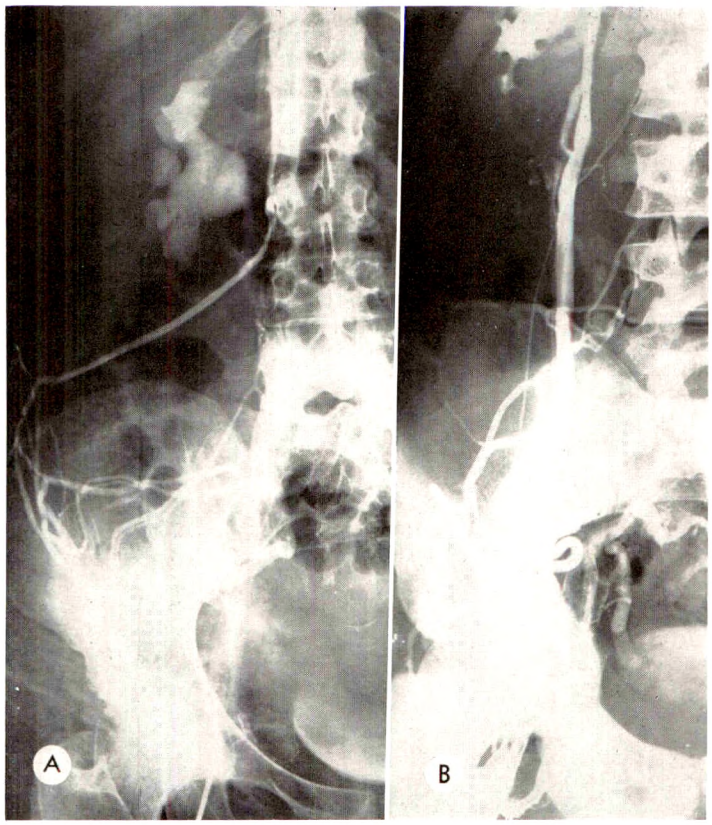


Fig. 17. External iliac vein obstruction may produce drainage into (*A*) the iliolumbar, ascending lumbar, and azygos systems or (*B*) into the spermatic vein.

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SIMPLIFIED TECHNIQUES IN THE EMPLOYMENT OF A ROTATIONAL COBALT 60 BEAM THERAPY UNIT*

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IF RADICAL treatment of small localized lesions by radiation therapy is to be successful, three basic requirements must be met. The first is an accurate knowledge of the location and extent of the volume to be treated. Secondly, a method must be devised which will permit the attainment of a satisfactory dose distribution which completely encloses this volume. Finally, this method must be employed to deliver an adequate cancerocidal dose in an optimum time to the volume in question. This paper deals with the second of these three requirements; *i.e.*, the attainment of an adequate dose distribution completely enclosing the tumor volume.

METHOD

The classic method of dose estimation as used in orthovoltage therapy (which shall be referred to here as "the per cent depth dose method") can be employed in cobalt 60 teletherapy with certain reasonable modifications. While in orthovoltage therapy the dose maximum is at the skin surface, in cobalt 60 teletherapy the maximum absorbed dose is at a depth of a few millimeters beneath the skin.[2,6] In the per cent depth dose method, the point on the central axis of the beam where the maximum dose is attained within the patient is used as a reference, and doses elsewhere are quoted as a percentage of the dose at this point. When this method is used in cobalt 60 teletherapy, the exposure dose rate is measured at a point in air which would correspond to a position 0.5 cm. beneath the presenting skin of the patient. Because of scatter from the diaphragm system, this exposure dose rate will be a function of the beam cross section. When the patient is placed in the beam, the absorbed dose rate at this point is given by the product of the exposure dose rate, the appropriate backscatter factor (which also depends upon the field area), and a factor[10] which serves to convert the exposure dose rate in roentgens per minute at this point to the absorbed dose rate in rads per minute. The absorbed dose rate at other points in the body is then found from the appropriate isodose distribution as a percentage of the maximum dose rate. In multiple field treatments, the dose at these points is merely the sum of the dose contributions from all the fields, and the over-all distribution within the patient is determined by summing the individual isodose distributions, which have been appropriately weighted for given dose.

This system of dosage estimation recommends itself for its simplicity, and it has stood the test of time in fixed field therapy. In rotation therapy, however, where the center of the tumor rather than the skin is placed at a fixed distance from the radiation source, the method becomes somewhat cumbersome. This is because the shape and nature of the isodose distribution are dependent on the source-to-skin distance, and in rotational or arc therapy this distance is continuously varying because of the anatomic contour. The method of "tumor-air ratios"[7,8] was developed to overcome this difficulty. In this *rotational* dosage system the exposure dose rate in air at the center of rotation as a function of beam cross section is first determined. The center of the volume to be treated is then placed at this point and the thickness of overlying tissue between the center and the skin surface is determined for an appropriate number of radii. Tumor-air ratio tables,[7,8,11] which express the ratio of absorbed dose in tissue to exposure dose in air as a function

* From The Ontario Cancer Foundation London Clinic, Victoria Hospital, London, Canada.

of depth of overlying tissue and field cross section, are then employed to determine the dose rate at the tumor when the beam axis is directed along each individual radius. If the rate of rotation is constant, the dose rates so determined can be averaged to give the effective dose rate during a cycle of arc or of full rotation.

The same principle can be used to advantage in stationary beam therapy. Figure 1 illustrates the method. The exposure dose rate in air at the center of rotation T is first determined as a function of beam cross section in the plane of T. When the patient is placed in the beam, the depth d of overlying tissue is determined either by a measurement on a body cross section or by the use of a calibrated front pointer attached to the head of the unit. The absorbed dose rate at T is then found by multiplying the known exposure dose rate by the appropriate tumor-air ratio as determined from the tables. The absorbed *dose* at T is given by the absorbed dose rate multiplied by the time of exposure. The absorbed dose at other points (*e.g.*, X) is then found by reference to the appropriate isodose distribution which is normalized to give 100 per cent[1,3,11] at the center of rotation T. The dose at T and X in multiple field distributions is then determined by summing the appropriate dose contributions from each field individually, and the over-all distribution is determined by the usual point-to-point method.

A number of advantages over more conventional methods become apparent when this approach is used with rotational types

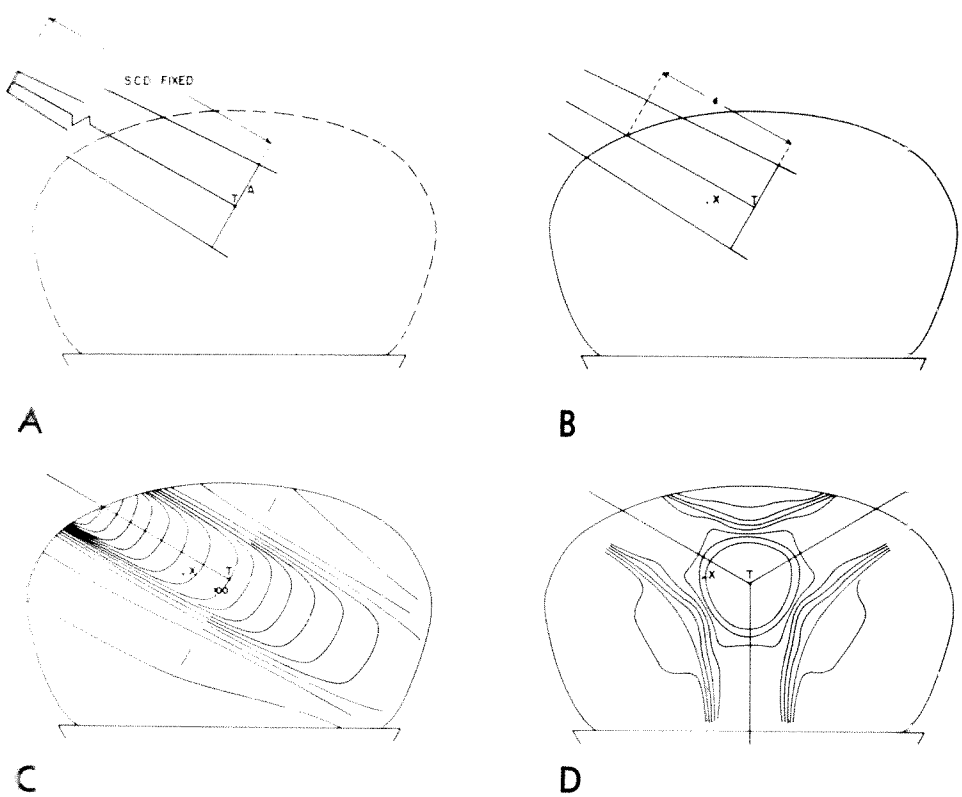


Fig. 1. Steps in dose estimation in fixed field therapy using the "tumor-air ratio" method. (*A*) Exposure dose rate at the center of rotation T is a function $E_T(A)$ of the area A of the beam in the plane of T. (*B*) Absorbed dose rate at T is $R_T(A, d) = E_T(A) \cdot T(A, d)$, where $T(A, d)$ is the appropriate tumor-air ratio. Absorbed dose at T is $D_T = R_T \cdot t$, where t is the time of exposure. (*C*) Absorbed dose at X is $D_x = D_T \cdot P$, where $P =$ (dose at X)/(dose at T). (*D*) Multiple field dose at T is $D_T = \sum_i D_{T_i}$ and at X is $D_x = \sum_i (D_{T_i} \cdot P_i)$.

of cobalt units. The first and most obvious advantage is that only one setting-up procedure is required, regardless of how many fields are to be used. This is because, with the patient placed so that the center of the treated volume is at the center of rotation, it is only necessary to rotate the unit from one entrance position to the next. On some types of rotational units this can be done from outside the treatment room. When the per cent depth dose method is used with this type of unit, each individual field must be set-up separately, with a consequent sacrifice of accuracy and time. Another advantage is that this approach focuses attention on the tumor volume to be treated, *i.e.*, the prescription of dose is to the tumor directly. The beam dimensions are chosen to enclose the tumor without reference to the area of the skin treated. While the dose delivered to the skin is readily calculable, it does not enter into the dosage prescription in the first instance. As has been pointed out, the method can be used with equal facility for fixed beam and arc therapy, and radically simplifies the determination of complete dose distributions, particularly in the use of wedge fields.

Du Sault[3] has discussed applications of this method in which a single isodose distribution[1] is used, regardless of the depth overlying the tumor center, on the assumption that the center lies in the region where the central axis depth dose curve is exponential. Corrections must be applied in the determination of the dose at points between the center and the skin, especially in the case of head and neck lesions where the skin-center distance is small.

The necessity for such corrections is eliminated if for each field size there is available a number of isodose distributions, each applicable to a range of skin-center distances. A satisfactory degree of accuracy can be attained by the use of three such distributions, measured with thicknesses overlying the center of 5, 10 and 15 cm. (Fig. 2). When the depth encountered clinically differs from these values, the isodose distribution for the nearest measured depth is employed. As seen in Figure 2, the error introduced by this approximation in the immediate region of the tumor is at most 2 per cent. Since the dose rate is determined accurately at the center of rotation by a method which is quite independent of

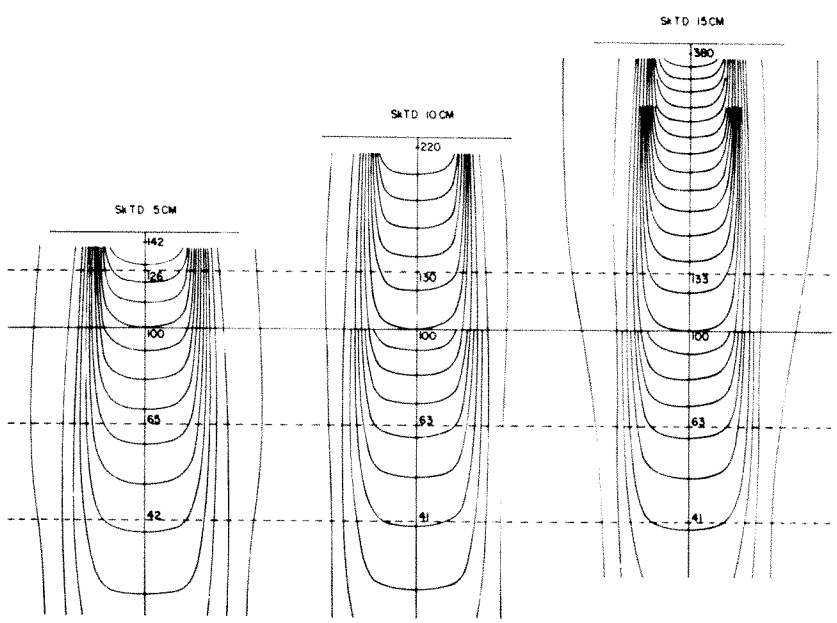


FIG. 2. Comparison of isodose distributions for a field of dimensions 6 cm. by 8 cm. at the center of rotation, with skin-tumor distance of 5, 10 and 15 cm. The distributions are normalized to 100 per cent at the center of rotation.

the isodose distribution, any error involved is a minimum in the volume of interest.

This fact is significant in that it makes possible the production of multiple field distributions without reference to any particular anatomic contour. That is, one can, at leisure, combine any number of fields directed at the center of rotation from different angles and so produce standard dose distributions of general usefulness. When such a standard distribution is applied to the contour of a particular patient, it will indicate with a high degree of accuracy the dose at points in the immediate vicinity of the tumor volume, and with somewhat less accuracy the dose at points remote from the center of the tumor. The inaccuracy over the whole of the range from the center of rotation out to the skin need not exceed 5 per cent under normal circumstances. Thus it is possible to build up a library of standard dose distributions which can be applied as required to dose computations involved in treatment. Such a library should contain dose distributions for multiple open fields, multiple wedge fields and moving beam therapy. Examples of such distributions are shown in Figures 3, 4, 5 and 6. Rotational and arc distributions can be calculated by the method of Gregory.[4]

The method is, then, to obtain an anatomic contour of the patient in the plane of treatment, to draw onto the anatomic contour the outlines of the tumor as established by roentgenographic or other methods, and then to choose the dose distribution from the ones available which will best enclose the tumor volume as drawn. An example is shown in Figure 7.

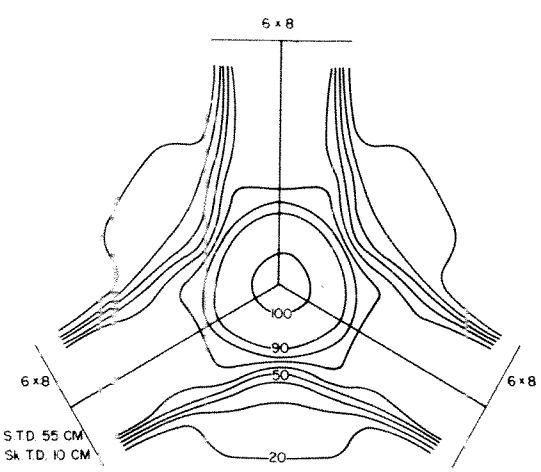


FIG. 3. Dose distribution for three 6×8 cm. fields at 120 degrees to one another. Source-tumor distance 55 cm.; skin-tumor distance 10 cm.

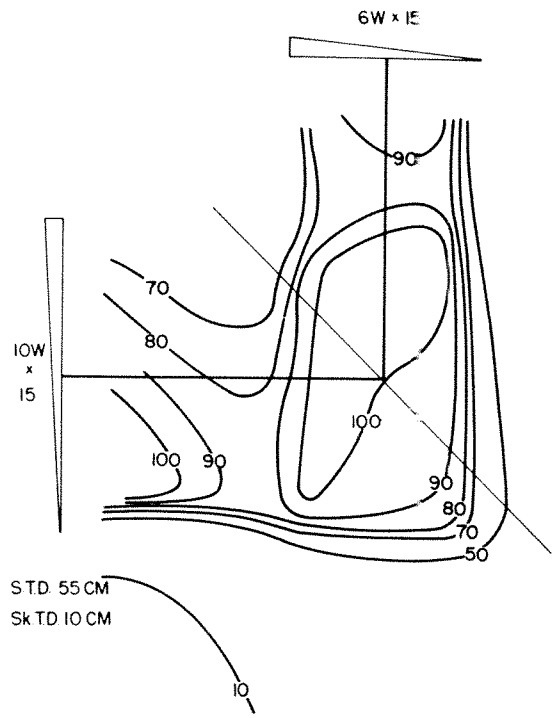


FIG. 4. Dose distribution for two wedge fields at 90 degrees. Left wedge 10 cm. wide; top wedge 6 cm. wide.

It is seen that the center of rotation need not necessarily coincide with the geometric center of the tumor, and that the contribution to the central dose need not be the same for all fields. From such a superposition it is possible to obtain the points on the skin at which the central axes of the individual beams are incident together with their relative directions. The depths d_1, d_2, and d_3 from the skin to the tumor on the central axes can either be measured on the contour as shown, or, when the patient is first set-up for treatment, they can be measured with a calibrated front pointer attached to the unit.

When one or more of the incident beams impinges upon the skin at other than normal incidence, it may be argued[5] that corrections must be made to the resulting

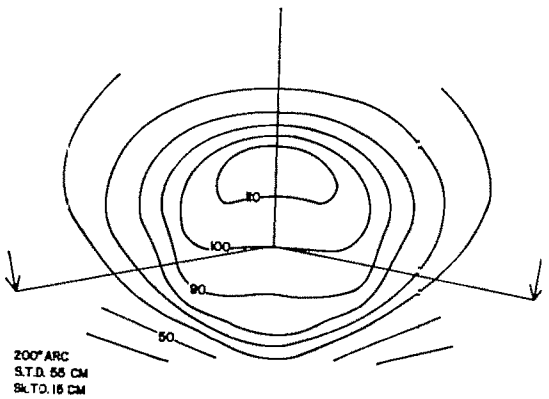


FIG. 5. Dose distribution for a 200 degree arc. Field size 10×12 cm.

isodose distribution to take into account the differential absorption on the two sides of the treatment field. An investigation into the alteration in the standard isodose patterns has shown that, while the patterns are undoubtedly modified somewhat due to this effect, the distortion of a multiple field isodose distribution is relatively minor provided the incident angles are not too extreme. This is illustrated in Figure 8 for the case of two wedge fields at right angles. In a similar way there will be a small amount of distortion in rotational and arc distributions due to the same effect. Again these distortions are relatively minor and have a negligible effect when the dose distribution is applied to the treatment of a particular patient.

The standard dose distributions are valid only in the plane of treatment, *i.e.*, in the

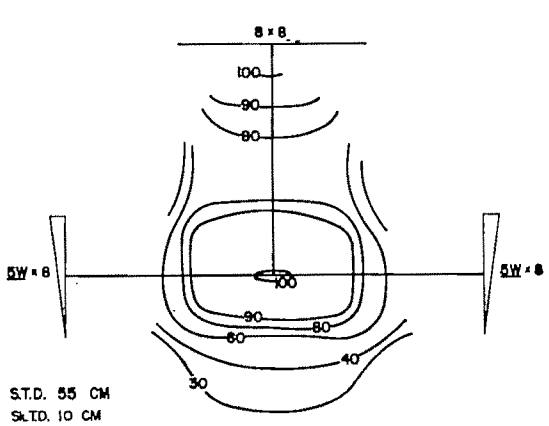


FIG. 6. Dose distribution for the combination of a single 8×8 cm. open field with two 5×8 cm. wedge fields.

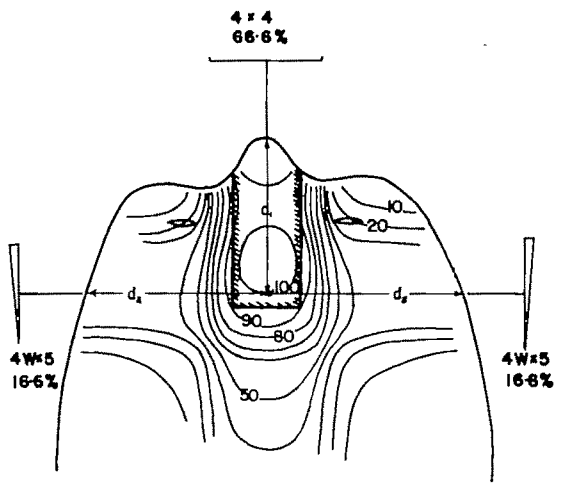


FIG. 7. Superposition of a standard dose distribution on a body cross section including the ethmoid sinuses. The 90 per cent dose contour encloses the treated volume.

plane containing the central axes of the individual beams. It is important to know the separation of the significant isodose surface in a direction perpendicular to this plane as a function of the field dimensions in this direction. Curves of the type shown in Figure 9 are useful in choosing the field dimensions which will be required to enclose the tumor.

It will be observed that, in the dose distributions of Figures 3, 4 and 6, the 100 per cent dose contour encompasses a very small volume whose shape is not necessarily

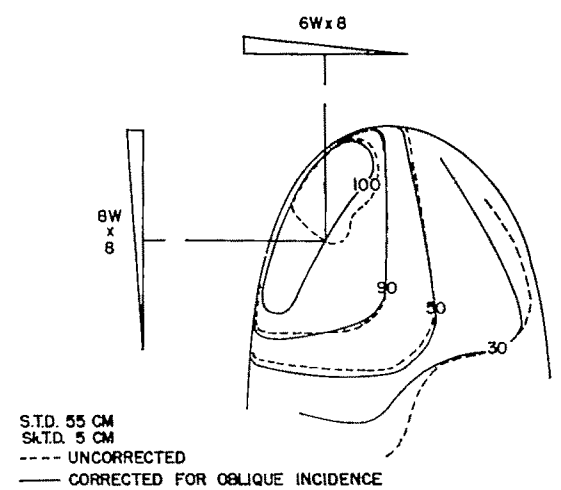


FIG. 8. A comparison of dose distributions for two wedge fields at 90 degrees, with and without correction for oblique incidence.

characteristic of the dose distribution as a whole. It is apparent that the 90 per cent contour approximates the nominal dimensions of the incident beams, and so field dimensions should be chosen which produce a distribution enclosing the known tumor volume within the 90 per cent contour. This choice implies the acceptance of a maximum dose within the tumor volume which is at least 11 per cent higher than that obtaining on the periphery of the tumor. This inhomogeneity within the tumor volume is, of course, characteristic of all such distributions regardless of the method of treatment and calculation used.

In practice, it is first necessary to know the desired position of the center of rotation with reference to skin marks on the exterior of the patient. The minimum number of such skin marks that will uniquely define such a point is three, and these marks should lie in a cross sectional plane through the center of the tumor. Figure 10 shows their relative relationship to one another and to the tumor center *T*. The line *BTD* passes through the center of the tumor and the line *AT* intersects it at right

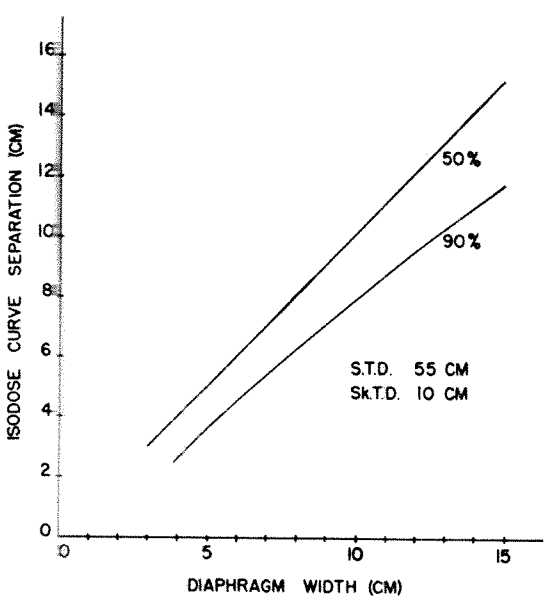


FIG. 9. Graph showing, as a function of diaphragm setting, the separation of the 90 and 50 per cent isodose surfaces at the center of rotation in a direction perpendicular to the plane of treatment. Theratron junior cobalt 60 unit; 1.5 cm. diameter source; source-center distance 55 cm.

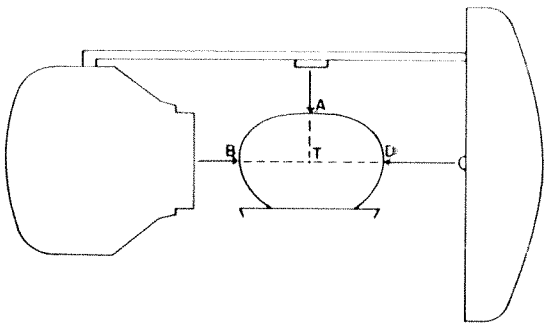


FIG. 10. Diagram illustrating the use of three light beams from the unit to place the point *T* at the center of rotation.

angles at the center. In order to use this method, it is necessary to have three directions defined from the unit itself. One of these directions may be defined by using the projection of the cross hairs in the light beam from the head of the unit. A back pointer light which directs a beam backward along the central axis in a direction toward the source defines the second of these directions, and a third light beam can be projected from a mounting similar to that shown in the figure in a direction at right angles to the line defined by the first two and intersecting this line at the center of rotation. Alternatively, since the center of rotation is a point fixed with reference to the walls of the treatment room, light beams can be projected from the walls and ceiling to meet at this point. With the patient supine or prone on the treatment stretcher, it is possible to position him in such a way that the three light beams impinge on the skin over the three skin marks. Since the beams intersect at the center of rotation, this procedure ensures that the appropriate point in the tumor is properly placed. The unit is then rotated to the desired treatment angle and the depth of tissue overlying the center of rotation along the central axis of the treatment beam is then measured, using a calibrated front pointer attached to the head of the unit. This depth is used to derive the dose rate at *T* for the appropriate field size by the use of tumor-air ratio tables.

In order to determine the absorbed dose rate at the center of rotation for a particular field, one must know the variation of

exposure dose rate with field size at the center of rotation and have available a table of tumor-air ratios appropriate to the particular treatment unit. It is possible to combine these data in the form of a single calculator.[9] In such a calculator the product of exposure dose rate variation at the center of rotation and the tumor-air ratio are plotted on full logarithmic paper as a function of field area, with depth of overlying tissue as parameter. The principle of the slide rule is used to calculate the treatment time for any particular tumor dose required.

SUMMARY

In summary, this paper describes a simplified method of tumor dose computation and isodose charting which is applicable to therapy units in which the radiation source is constrained to move in a circle with the central axis of the beam pointing at a fixed point in space. The method of tumor-air ratios is employed to determine the dose rate at a point in the volume to be treated, in both moving field and stationary field techniques. Isodose charts which are normalized to 100 per cent at the center of rotation are then employed to determine the dose rate at other points within the treatment field. Using this method, it is possible to build up a library of standard dose distributions for stationary, wedge and rotational treatments which can be used directly to indicate the dose distributions within individual patients. It is seen that by the use of such standard distributions a large amount of very tedious computation is eliminated, and complete isodose charting for each patient treated can now become the rule rather than the exception. Since the errors involved in the use of these standard distributions are well within the uncertainties otherwise inherent in radiation therapy, the method permits of great simplification in treatment planning without a significant sacrifice in accuracy. The interchange of precalculated dose distributions between institutions employing the same type of unit becomes an attractive possibility.

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The methods described in this paper are the result of the joint efforts of the physics and radiotherapeutic staff of this Clinic. The library of standard distributions has been built up through the work of Mr. P. M. Pfalzner and Dr. H. I. S. Ferguson.

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THIMBLE CHAMBER CORRECTIONS BELOW 100 KV. EFFECTIVE

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IT IS well known that thimble ionization chambers will give erroneous results if used to measure roentgen-ray beams outside of the useful energy range designated by the manufacturers. Unfortunately, the meaning of the manufacturer's statement, "Good for energies from 30 to 400 kv. effective," is frequently misinterpreted by those using this instrument when measuring dosage in superficial therapy. It is the intention of this paper to draw attention to this common misinterpretation in order to: (1) stimulate interest, leading to further investigations by those laboratories adequately equipped to study this problem; (2) encourage the widespread dissemination of existing information on this problem; (3) elucidate the meaning of the manufacturer's claims; and (4) improve dosage specification in superficial therapy.

If a typical response curve for thimble ionization chambers as reported by the manufacturer is presented in terms of half value layer, as shown in Figure 1, the inadequacy of this equipment for the measurement of superficial therapy beams becomes obvious.

In addition to the data supplied by the manufacturers, some data are available in the literature.[1,2] The data of these authors have been rearranged and plotted along with those from two manufacturers and are shown in Figure 2. The method of converting these data can be deduced from the data presented in Table 1.

Although the curves of Figure 2 may not be applicable to any one r-meter, they may serve as a temporary guide for those who at present do not employ any correction factor in this range. Most superficial ther-

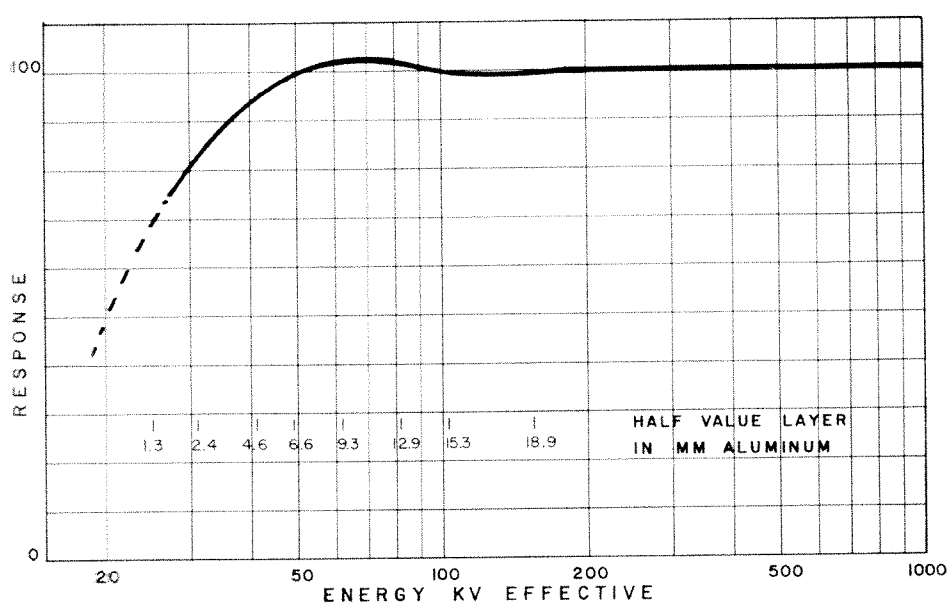


FIG. 1. Typical response curve of a Landsverk model L-64 r-meter as reported by the manufacturer. Half value layers have been calculated by the author. The manufacturer stresses that "special attention is given to calibrations in the energy ranges most commonly used in x-ray and radium therapy." Victoreen's typical response curve is similar. (Published with permission from the Landsverk Electrometer Company.)

TABLE I

CORRECTION FACTORS

kv. Effective	Effective Wavelength Angstroms	μ/ρ	Half Value Layer mm. Al	Correction Factors	
				Victoreen	Landsverk
82	0.15	.198	12.9	.99	.99
62	0.2	.274	9.3	.98	1.00
49	0.25	.388	6.6	.99	1.01
41	0.3	.557	4.6	1.00	1.06
31	0.4	1.09	2.4	1.02	1.22
25	0.5	1.95	1.3	1.05	1.43
21	0.6	3.22	0.8	1.08	—
15	0.8	7.32	0.35	1.22	—

The data of columns 1, 2, and 3 are obtained from Table 2.6 of Handbook of Radiology, R. H. Morgan and K. E. Corrigan. The Year Book Publishers, Inc., Chicago, 1955.

Column 4 was calculated on the basis of simple exponential absorption.

The values of column 6 were obtained from Landsverk's typical response curve which is shown in Figure 1. Victoreen's values were obtained from typical response curve for Model 70-5 Chamber, Victoreen Instrument Company, personal communication, August, 1960.

apy equipment comes within this scope, as is shown by the typical half value layers listed in Table II.

Those desiring more than a temporary guide constructed from data in the literature must have their equipment calibrated by the National Bureau of Standards where, according to Title 15, chapter II, part 204 of the Federal Register, calibration at 4 half value layers in this range can be sup-

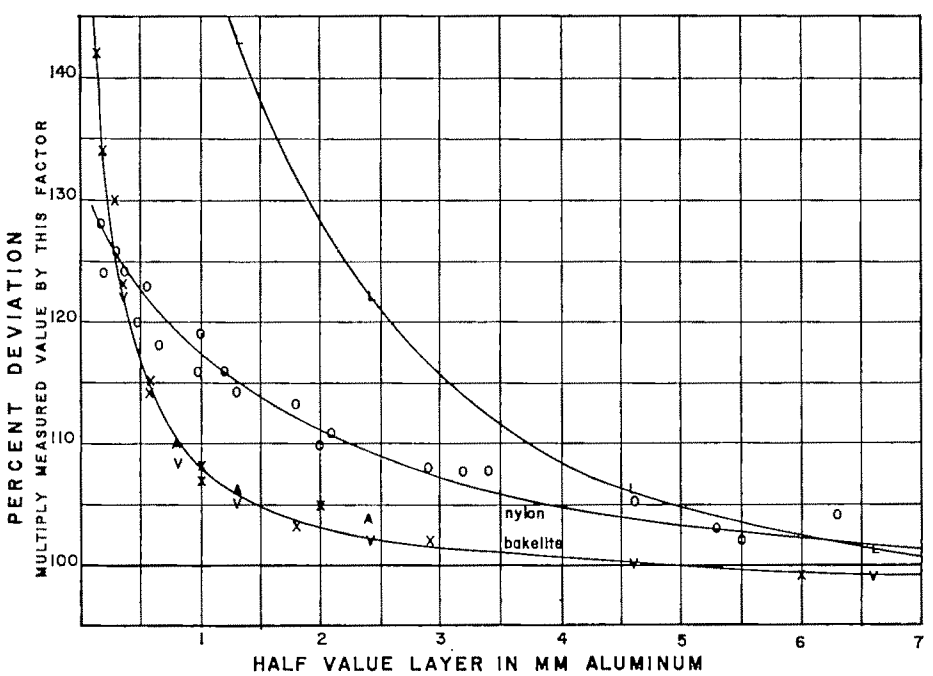


FIG. 2. R-meter correction factors for Victoreen nylon and bakelite probes and the Landsverk L-120 series probes. It is possible that the curves are more closely related to chamber size than composition. The plotted points were obtained from the following sources: X and O, Day;[1] A, Victoreen *et al.*;[2] L, Landsverk Electrometer Company brochure; V, Victoreen Instrument Company, personal communication, August, 1960.

TABLE II

TYPICAL HALF VALUE LAYERS FOR SUPERFICIAL ROENTGEN THERAPY EQUIPMENT

Manufacturer	kv.	Added Filter	HVL mm. Al
Picker	74	none	0.65
		1 mm. Al	1.3
	120	none	0.8
		1 mm. Al	2.0
		3 mm. Al	3.6
Keleket	60	none	0.85
	100	none	1.3
		2 mm. Al	3.4
General Electric (KX-10)	70	none	1.4
	100	none	1.8
	125	3 mm. Al	4.0

These data were obtained from calibration charts in our file.

plied for a 25 r chamber only. The individual user must then provide his own secondary calibration on other chambers.

SUMMARY

While this paper does not give new data on this problem, it does present existing data in a more utilitarian form and brings attention to the necessity of correcting r-chamber measurements in the calibration of output from superficial roentgen therapy apparatus. These corrections, when properly applied, should improve the specification of dosage.

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THE EFFECTS OF CARDIAC IRRADIATION UPON THE NORMAL CANINE HEART*

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CARDIAC irradiation has been proposed as a possible therapeutic method for inducing an increase in myocardial vascularity in coronary artery disease. In earlier publications[9,10,11] electrocardiographic and physiologic data obtained from a study of animals subjected to cardiac irradiation as well as an evaluation of the survival of such animals following acute coronary artery ligation have been presented. These studies have shown that the irradiated dogs withstand the acute myocardial insult of coronary ligation better than the nonirradiated control animals both in terms of survival and increased intercoronary anastomotic blood flow.

It is the purpose of this study to present a pathologic analysis of the effects of various dosages of radiation upon the canine heart and adjacent organs and tissues after varying periods of time. Dogs subjected to coronary artery ligation subsequent to irradiation as well as nonligated animals were studied.

METHOD

One hundred and fifteen mongrel dogs were used in this study. Thirty dogs received no irradiation and served as normal control animals. The remaining 85 animals were given varying doses of radiation and were studied at intervals of up to one year post irradiation (Table 1).

Cardiac irradiation was performed in the following manner. Of each dog a scout roentgenogram of the chest was taken to determine the heart location and size. This field was then mapped on the dog's thorax on both the left and right sides. The heart was irradiated by means of three treatments to the left chest field and two to the right chest field during a fourteen to seventeen day period. The treatments were given with a parallel opposing pair of fields ranging in size from 80–120 sq. cm. The average separation of the fields was 10 cm. Two hundred kilovolt roentgen rays which, after filtration, had a half value layer of 0.9 mm. of copper were utilized at a focal skin distance of 50 cm. The calculated dose to the heart in one group was 1,300 r (1,500 in air). Another group received a heart dose of 2,000 r (2,500 in air). A third group received a heart dose of 2,700 r (3,600 in air). This latter group received treatments in a manner similar to the other groups with the exception that three treatments were given to each chest field and the source of radiation was a cobalt 60 teletherapy unit.

Four to six days following the termination of the radiation treatments, one group of dogs was subjected to coronary artery ligation. Those dogs surviving this procedure were sacrificed two, four and six months post ligation for pathologic study. Those dogs which did not survive ligation or died within two months post ligation were also studied. The hearts were studied by injection of barium sulfate into the coronary orifices to outline the grossly functioning coronary circulation. Roentgenograms of the injected specimens were taken.[4] The hearts were then fixed in formalin and multiple transverse sections of the entire heart were made for gross and microscopic analysis. Some of the hearts were injected with vinylite plastic and corrosion prepara-

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TABLE I

EXPERIMENTAL FACTORS IN CARDIAC IRRADIATION STUDY

Group	No. of Days	Estimated Dose to Myocardium (r)	Total Dose in Air (r)	Time of Pathologic Study
Control	30	0	0	Immediately—2 mo. post coronary artery ligation
Irradiated-ligated (coronary artery ligated 4–6 days post irradiation)	25	1,300	1,500	Immediately—6 mo. post coronary artery ligation
	25	2,000	2,500	Immediately—6 mo. post coronary artery ligation
Irradiated—ligated (coronary artery ligated 6 months post irradiation)	13	1,300 and 2,000	1,500 and 2,500	Immediately—2 mo. post coronary artery ligation
	3	2,700	3,600	Immediately—24 hr. post coronary artery ligation
Irradiated—nonligated	14	400–2,700	500–3,600	Several hours post first treatment—6 mo. post termination of radiation therapy
	5	2,100–2,700	2,700–3,600	One year post termination of radiation therapy

tions of the entire coronary circulation were made.[7] Sections of the sternum and rib cage were taken for bone marrow study. The lungs and mediastinal esophagus were also examined.

Another group of dogs, similarly irradiated, received no further treatment for a period of six months, after which it was subjected to coronary artery ligation. Similar studies were also performed on these animals. There was also a group of dogs (irradiated-nonligated) consisting of those animals which died of causes unrelated to the irradiation either during the course of irradiation or prior to the time of ligation. Postmortem and pathologic studies were performed on these animals.

In order to evaluate the possible late effects of irradiation, a group of 5 dogs was irradiated in a similar manner with dosages of 2,700–3,600 r in air (estimated 2,100–2,700 r to the myocardium). Prior to irradiation, weights, chest roentgenograms, electrocardiograms, hemoglobin, hematocrit, white blood cell counts and peripheral smears were obtained for use as baseline values. Nothing further was done for a period of one year. At the termination of this period, the dogs were again weighed and repeat roentgenograms, electrocardiograms and blood studies were performed. In addition, bone marrow from the iliac crest was examined in each dog. Following these studies the animals were sacrificed, and their organs examined grossly and microscopically.

RESULTS

A. BARIUM INJECTION STUDIES

Injection of the hearts of nonirradiated control dogs dying in the first twenty-four hours post ligation revealed the absence of barium in the anterior descending branch of the left coronary artery and its branches distal to the ligature applied at operation (Fig. 1*A*). The barium entered the right coronary and left circumflex coronary arteries and their branches, but did not

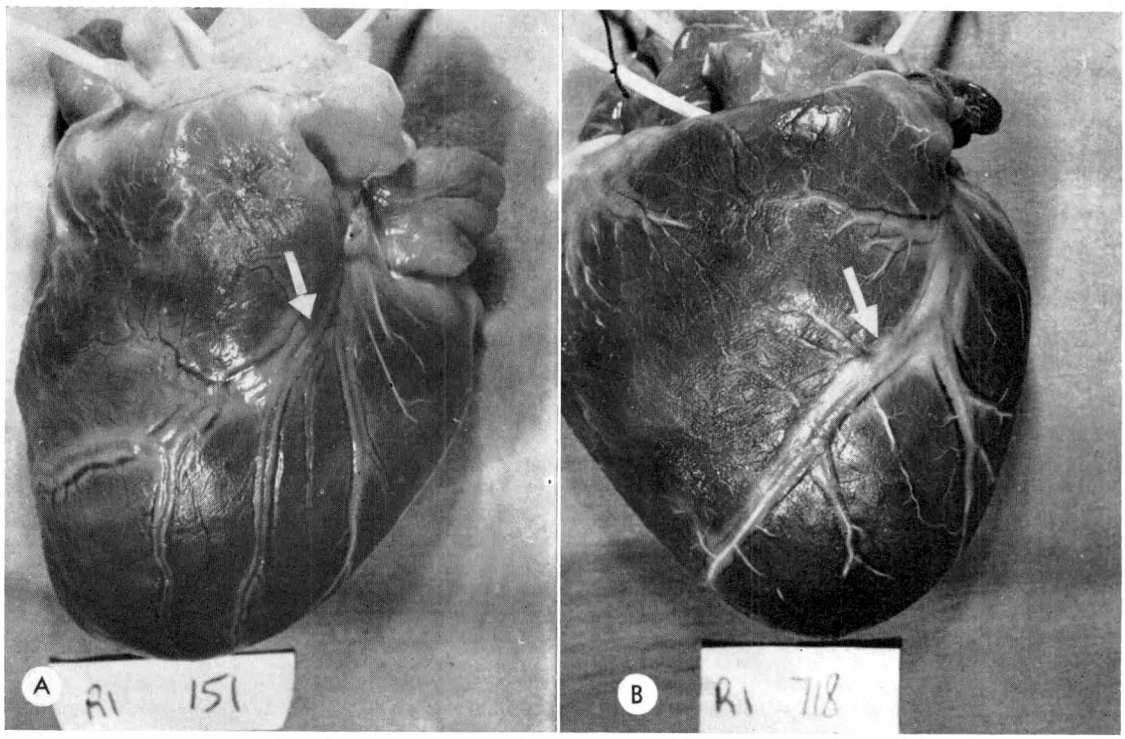


FIG. 1. (*A*) Anterior view of the heart of a nonirradiated dog dying one hour post ligation of the anterior descending coronary artery (arrow). Barium has been injected into the coronary orifices. Note the absence of barium in the ligated vessel and its branches. (*B*) Similarly injected heart of irradiated dog. Barium is seen in the anterior descending coronary artery and its branches.

anastomose with or enter the region of the heart supplied by the anterior descending coronary artery (Fig. 2*A*). Study of the irradiated hearts of similar dogs revealed a range of conditions varying from lack of filling of the anterior descending coronary artery to almost complete filling of the vessel (Fig. 1*B*) by retrograde flow of barium from branches of the left circumflex artery (Fig. 2, *B* and *C*). Control dogs dying twenty-nine hours and four days post ligation showed only slight to moderate retrograde filling of the anterior descending coronary artery and its branches; however, those control dogs surviving one to two months post ligation exhibited good filling of the ligated vessel. In comparison, the hearts of irradiated dogs dying four, ten and forty-two days post ligation revealed good to excellent filling of the anterior descending coronary artery up to the point of ligation by retrograde flow of barium through anastomotic connections between the ligated vessel branches and the adjacent intact coronary circulation. The hearts of irradiated dogs surviving two to six months exhibited excellent retrograde filling of the area of infarction and appeared more vascular than the normal heart.

B. ROENTGEN FINDINGS

Roentgenographic findings of the injected hearts corresponded to the gross observations mentioned above. In control dogs dying within twenty-four hours, a large avascular area was seen in the region of the distribution of the ligated coronary artery (Fig. 3*A*). This avascular area was not observed as frequently and did not appear as avascular on roentgenograms of comparable irradiated heart specimens (Fig. 3*B*). Roentgenograms of irradiated hearts two to six months post ligation demonstrated marked vascularity.

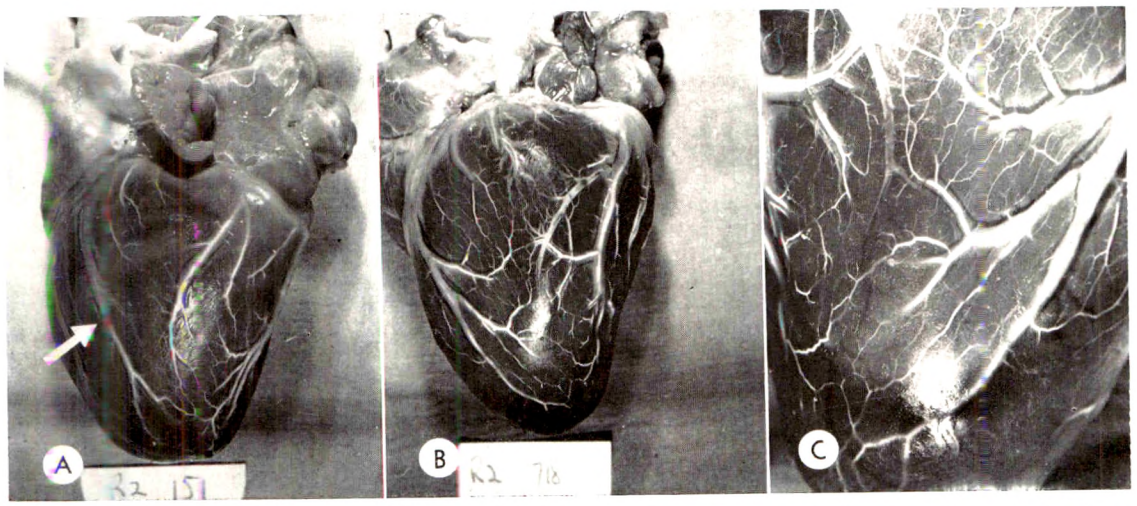


FIG. 2. (*A*) Lateral view of a barium injected nonirradiated heart. Arrow points to bare area (devoid of barium) corresponding to the distribution of the previously ligated anterior descending coronary artery. No significant intercoronary anastomoses are seen between the ligated vessel and the left circumflex artery which contains barium. (*B*) Similarly injected irradiated heart. Note the presence of numerous barium filled anastomotic connections between the anterior descending and left circumflex coronary arteries. (*C*) Close-up of area of intercoronary anastomoses seen in *B*.

C. CORROSION PREPARATION STUDIES

Corrosion preparations of hearts injected with vinylite demonstrated well the difference in vascularity between control and irradiated hearts. Figure 4*A* shows the vascular pattern of the normal heart. Figure 4*B* shows such a heart which has been subjected to ligation of the anterior descending coronary artery. This has created a large avascular area corresponding to the distribution of the ligated vessel. Figure 4*C* shows an irradiated heart one-half hour post ligation. This heart is similar to the normal nonligated heart in vascularity. An avascular area is not seen. The distribution of the anterior descending coronary artery has been completely filled by plastic material flowing through anastomotic channels from both right and left coronary artery branches.

D. GROSS AND MICROSCOPIC STUDIES—PATTERN OF INFARCTION

There was no distinct gross difference between the hearts of irradiated and control dogs in regard to the distribution of the infarcted area. In dogs surviving coronary artery ligation, the area of infarction usually involved most of the anterior wall of the left ventricle and the left border of the right ventricle. However, an analysis of the transverse sections of the hearts revealed an impressive contrast. All control animals presented infarcted cardiac muscle involving the entire thickness of the ventricular wall (Fig. 5 *A* and 6 *A*). Irradiated dogs of equal survival periods did not exhibit this "through and through" infarction of the ventricular wall, but instead had spared areas consisting of varying thicknesses of normal heart muscle in the subepicardium throughout the extent of the infarction (Fig. 5 *B* and 6*B*). There was no difference noted in the endocardial distribution of the infarction.

Microscopic sections taken from the region of infarction in the control hearts revealed complete necrosis of the ventricular wall (Fig. 7*A*). Sections of equivalent irradiated dogs' hearts exhibited necrosis plus a superficial area of normal muscle (Fig. 7*B*). Healing (fibroblastic proliferation) begins in this spared area of myocardium as early as four days post infarction while complete necrosis is still present in the center of the infarction. The sections

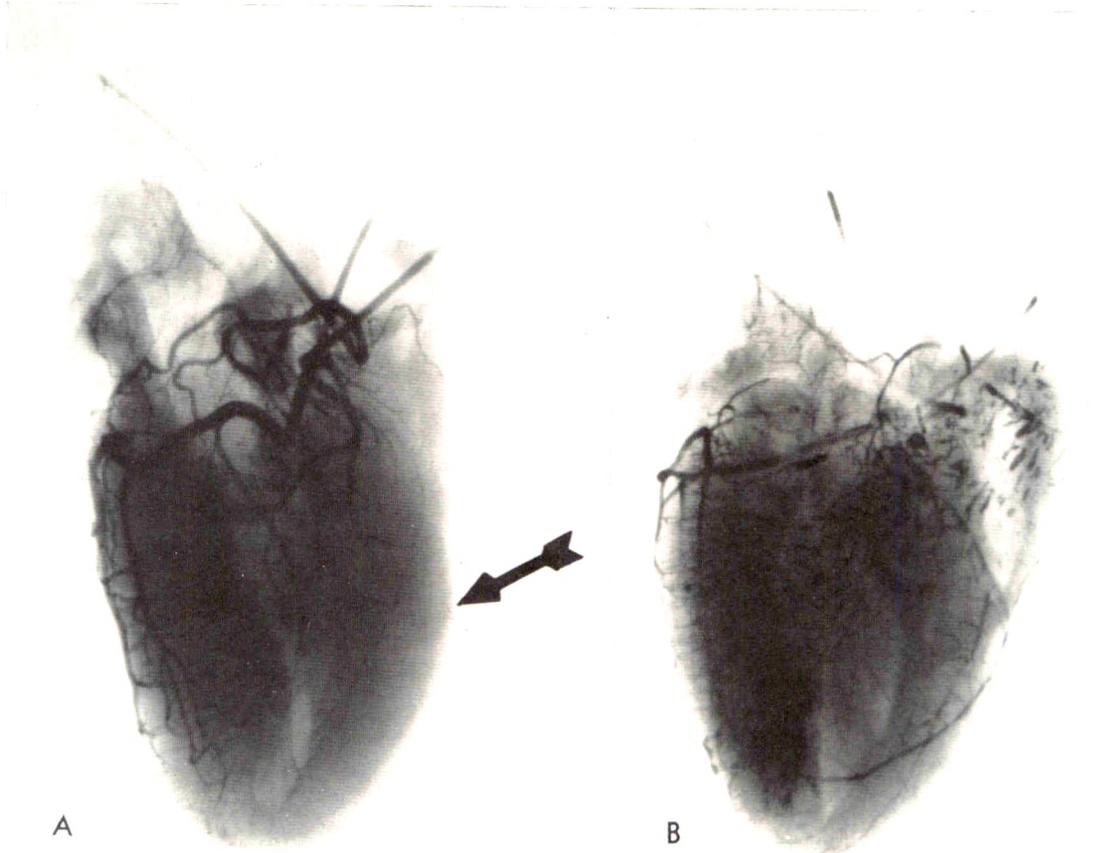


Fig. 3. (*A*) Roentgenogram of barium injected nonirradiated heart. Arrow indicates avascular area corresponding to the distribution of the previously ligated anterior descending coronary artery. (*B*) Roentgenogram of barium injected irradiated heart. The heart appears vascular. Note the absence of the avascular area seen in the region of the ligated vessel in the nonirradiated heart.

through the area of infarction in control dogs did not show this fibroblastic proliferation in the region of the subepicardium as there is no normal myocardial tissue from which this can occur. Only the viable tissue adjacent to the necrotic area of infarction exhibited fibroblastic proliferation in the control animals. A greater frequency of calcium deposition was seen in the area of infarction in the hearts of control animals one month or more following infarction.

E. RADIATION DAMAGE

There was no evidence of myocardial necrosis attributable to the effects of radiation in any of the irradiated hearts examined. An inflammatory response of pericarditis or myocarditis was not seen. There was no evidence of the formation of granulation tissue or myocardial fibrosis resulting from the cardiac irradiation. No evidence of obliteration of pulmonary or coronary vessels due to irradiation was seen on gross or microscopic analysis.

Examination of the lungs revealed the presence of a focal radiation induced pleuritis with subsequent pleural thickening in some of the irradiated animals. This effect was rarely seen in dogs receiving 1,500 r in air to the chest region. Those dogs receiving 2,500 r and 3,600 r to the chest region exhibited these findings fairly consistently six months post irradiation. These changes were not seen in the animals studied seven to twenty-four days following the termination of their treatments. The pleuritis in-

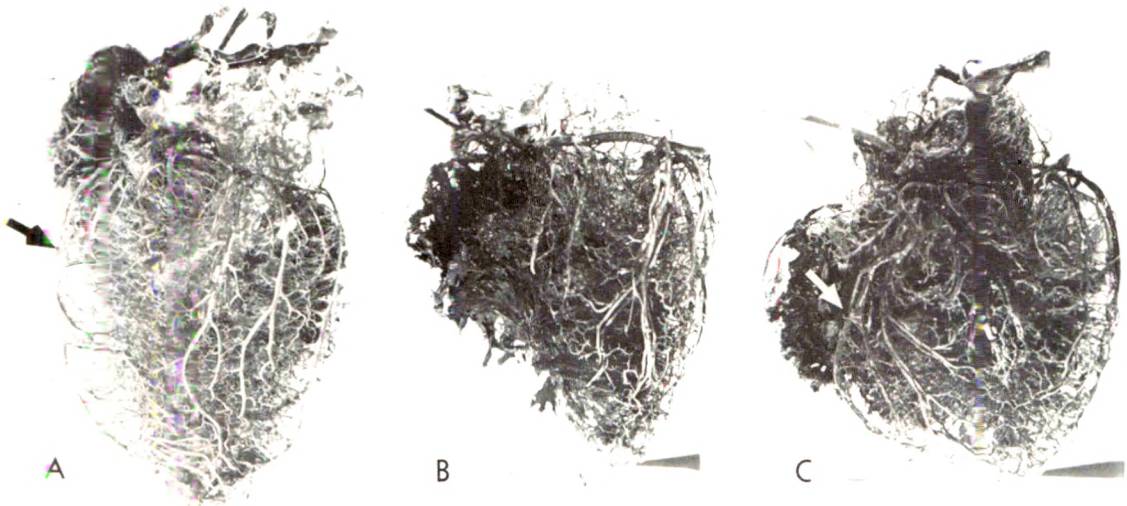


FIG. 4. (*A*) Vinylite injection and corrosion specimen of normal coronary circulation (lateral view). Arrow points to the anterior descending coronary artery. (*B*) Specimen of nonirradiated heart one-half hour post ligation of the anterior descending coronary artery. Note segment of absent coronary circulation which corresponds to distribution of the ligated vessel. (*C*) Specimen of irradiated heart one-half hour post ligation of the anterior descending coronary artery. The pattern of vascularity resembles a normal nonligated heart. Anterior descending coronary artery (arrow) has filled in a retrograde fashion by means of functioning intercoronary anastomotic channels.

volved only the area of lung underlying the field of irradiation and consisted grossly of patchy areas of grayish white pleural thickening (Fig. 8*A*). The lung tissue at a distance from the irradiated field appeared normal. Not all dogs receiving the same amount of irradiation showed the same degree of pleural involvement. Microscopic sections (Fig. 8*B*) revealed pleural fibrosis which in some cases involved several millimeters of the underlying lung parenchyma. The elastic membrane of the pleura was intact. There were no indications by physical or pathologic examination of any pulmonary effects of the radiation therapy sufficient to interfere with normal respiratory function. Examination of

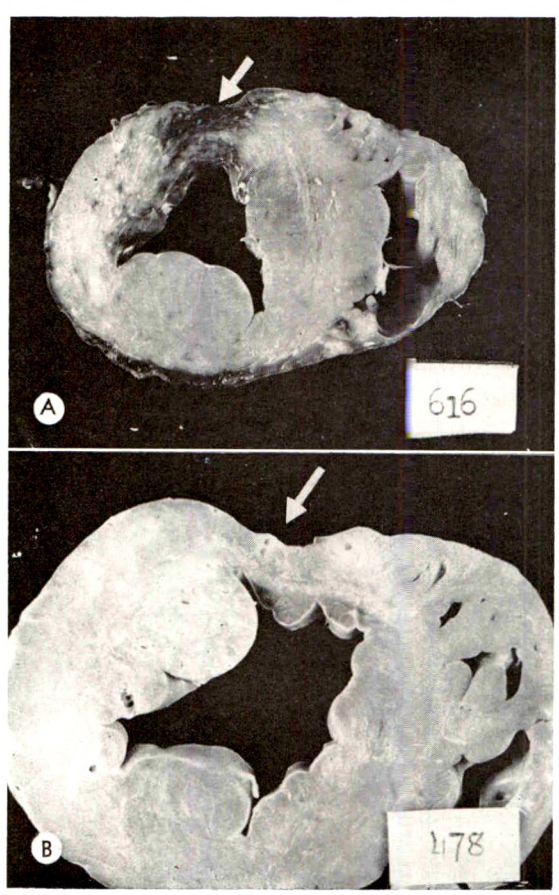


FIG. 5. (*A*) Transverse section of nonirradiated heart two months post ligation of anterior descending coronary artery. Arrow indicates area of "through and through" infarction in the anterior wall of the left ventricle. (*B*) Comparable transverse section of irradiated heart (2,000 r). Arrow indicates area of spared normal muscle overlying area of infarction.

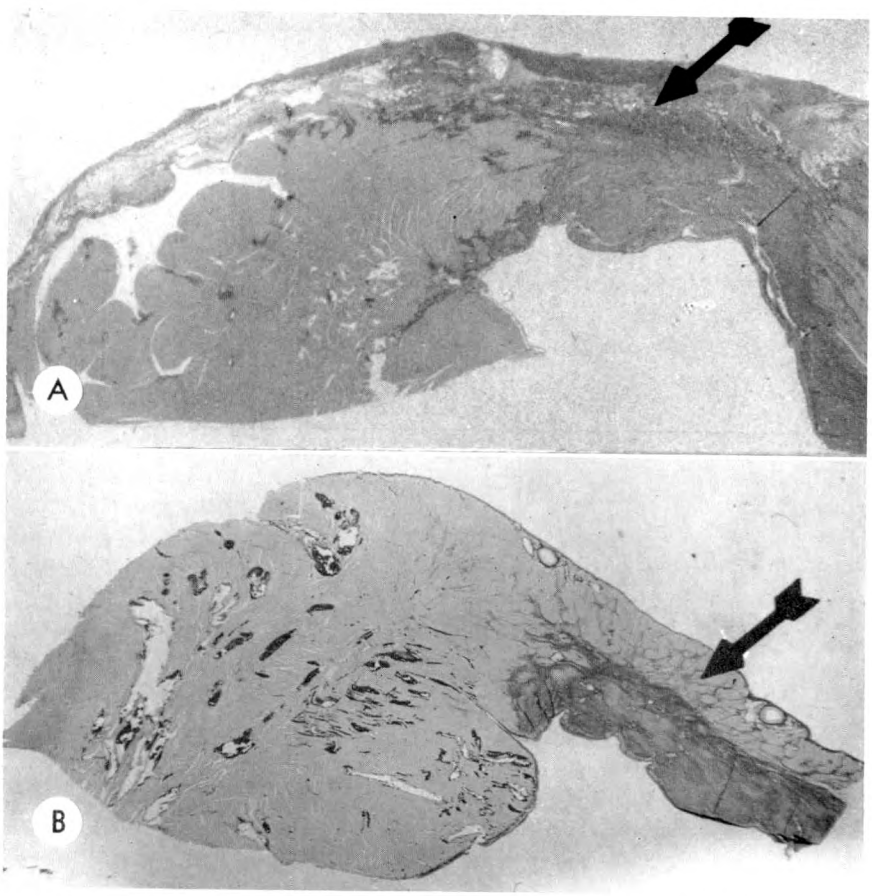


FIG. 6. (*A*) Van Gieson stained section through area of infarction in nonirradiated heart two months post ligation. Arrow indicates area of infarction extending from endocardial to epicardial surface. (*B*) Comparable section of area of infarction in an irradiated heart (2,000 r). Arrow points to normal muscle overlying the area of infarction. Note the presence of vessels in this area.

the lungs of nonirradiated dogs subjected to thoracotomy six months previously revealed, in many cases, pleural thickening of equal or greater severity than that seen in the irradiated animals. The pleural thickening did not, however, extend into the lung parenchyma in the nonirradiated animals.

Examination of the bone marrow taken from the ribs and sternum of irradiated animals revealed the following findings: Dogs receiving 1,500 r exhibited normal to moderate hypocellular marrow at six months post irradiation. Dogs receiving 2,500 r and 3,600 r exhibited moderate to marked focal hypocellular marrow changes six months post irradiation. In several dogs receiving 3,600 r, focal fibrosis was also noted. The most pronounced effects were seen in the direct field of irradiation (Fig. 9*A*). Sections taken from areas away from the irradiated field (Fig. 9*B*) showed normal hematopoiesis.

Other tissues in the irradiated dogs consisting of the mediastinal structures (trachea, esophagus, aorta) as well as stomach, small intestine, liver, spleen and kidney were examined. No changes in these were seen.

The results of studies performed one year post irradiation on those animals which received no surgery or other treatment were as follows:

1. All dogs maintained their pre-irradiation weight.

2. Chest roentgenograms and electro-

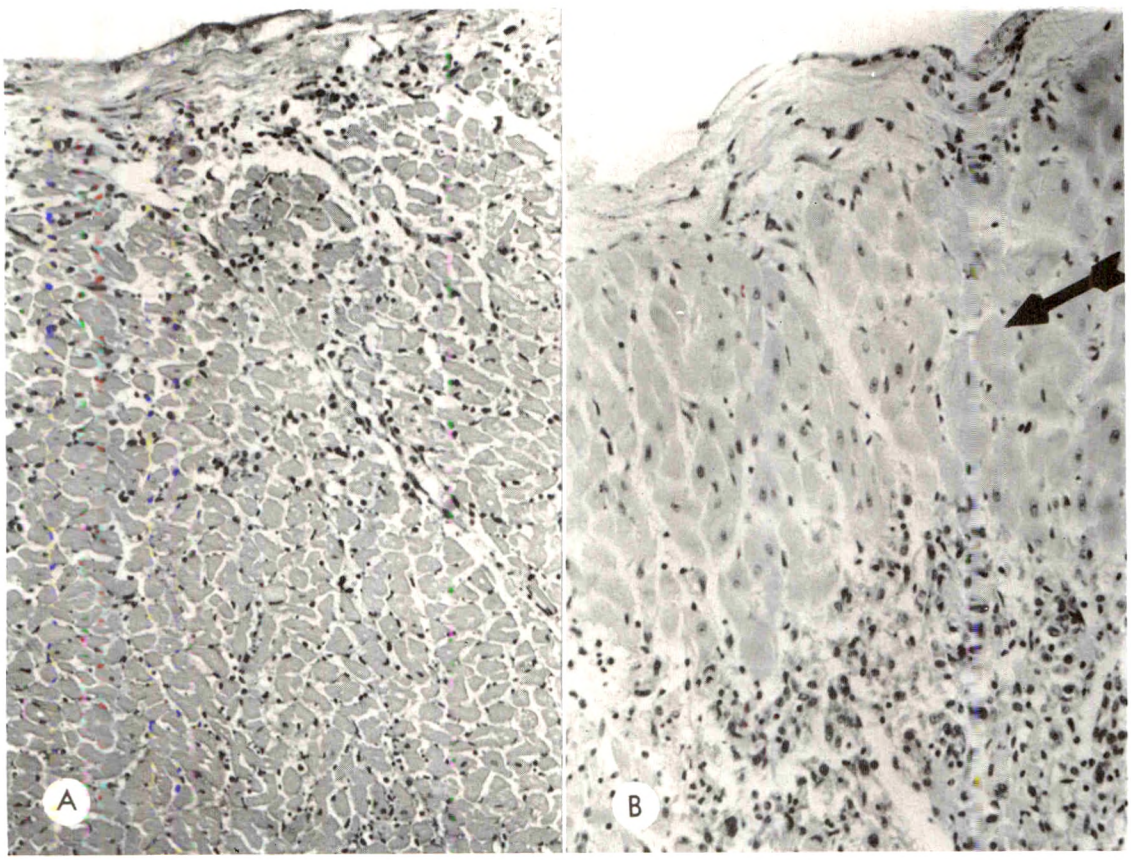


Fig. 7. (*A*) Photomicrograph of a section of infarcted ventricular wall in nonirradiated heart seven days post ligation of the anterior descending coronary artery. Necrosis extends to the epicardial surface. Hematoxylin-eosin stain ×196. (*B*) Comparable section of irradiated heart. Arrow is in region of spared normal muscle in subepicardium.

cardiograms showed no significant changes.

3. Blood studies (hemoglobin, hematocrit, white blood cell count, peripheral smear and iliac crest marrow examinations) showed no significant alterations, and were within normal limits.

4. All dogs were in good health when they were sacrificed.

5. Gross and microscopic findings revealed patchy areas of pleural thickening of both lungs underlying the portals of irradiation. There was no pleural effusion or evidence of radiation pneumonitis or pulmonary fibrosis.

6. No pericarditis, pericardial effusions, or gross myocardial damage was seen.

7. The coronary vessels were not obliterated.

8. The esophagus was grossly unremarkable (microscopic sections were taken and confirmed the above gross finding).

9. Sternal marrow in the irradiated area was as previously described. Normal hematopoiesis was seen in marrow obtained away from the irradiated area.

DISCUSSION

Previous studies[9,10,11] have shown that dogs receiving cardiac irradiation prior to left anterior descending coronary artery ligation have a higher rate of survival and greater intercoronary anastomotic blood flow than do nonirradiated animals. A pathologic analysis of equivalent irradiated and nonirradiated hearts is of great help in understanding the cause of the increase in the survival rate and in the coronary blood flow. Although the normal pattern of

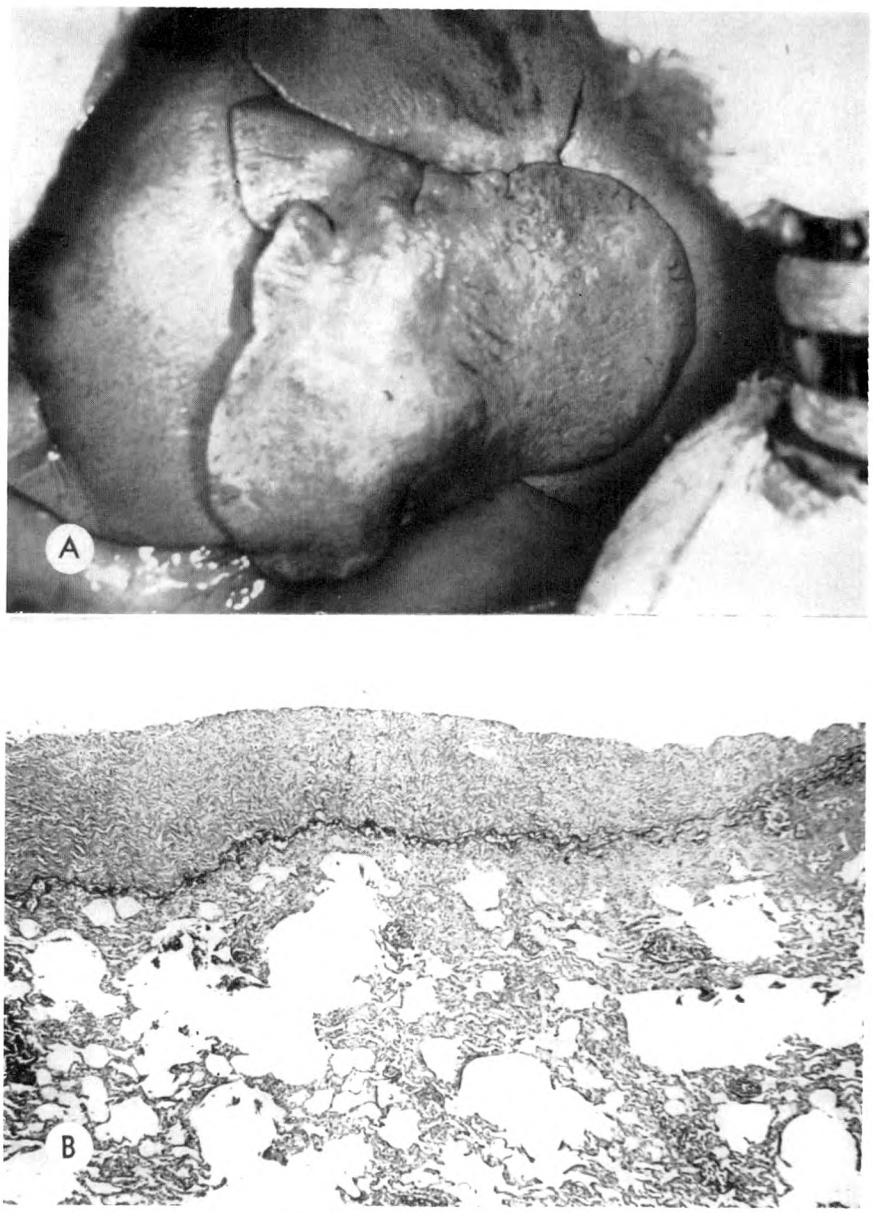


FIG. 8. (*A*) Photograph of dog's lungs taken at time of thoracotomy six months post irradiation (3,600 r). Several areas of pleural thickening are present. These changes are limited to the area of irradiation. The remaining pleural surfaces appear normal. (*B*) Photomicrograph of section of lung tissue underlying the field of irradiation (3,600 r) six months post irradiation. Note pleural thickening and small area of subpleural fibrosis. The elastic membrane of the pleura is intact. The remainder of the underlying lung tissue appears normal. Hematoxylin-eosin stain ×58.

coronary artery distribution to the heart physiologically amounts to an end arterial system,[12] anatomically the terminal ramifications of the coronary arteries are in mutual cross communication by way of a network of minute intercoronary vascular channels.[3,8,13] Husni and Simeone[5] reported that the changes associated with the formation of collateral circulation in the myocardium when a major artery is occluded are, for the most part, attributable to the establishment of an increased gradient of pres-

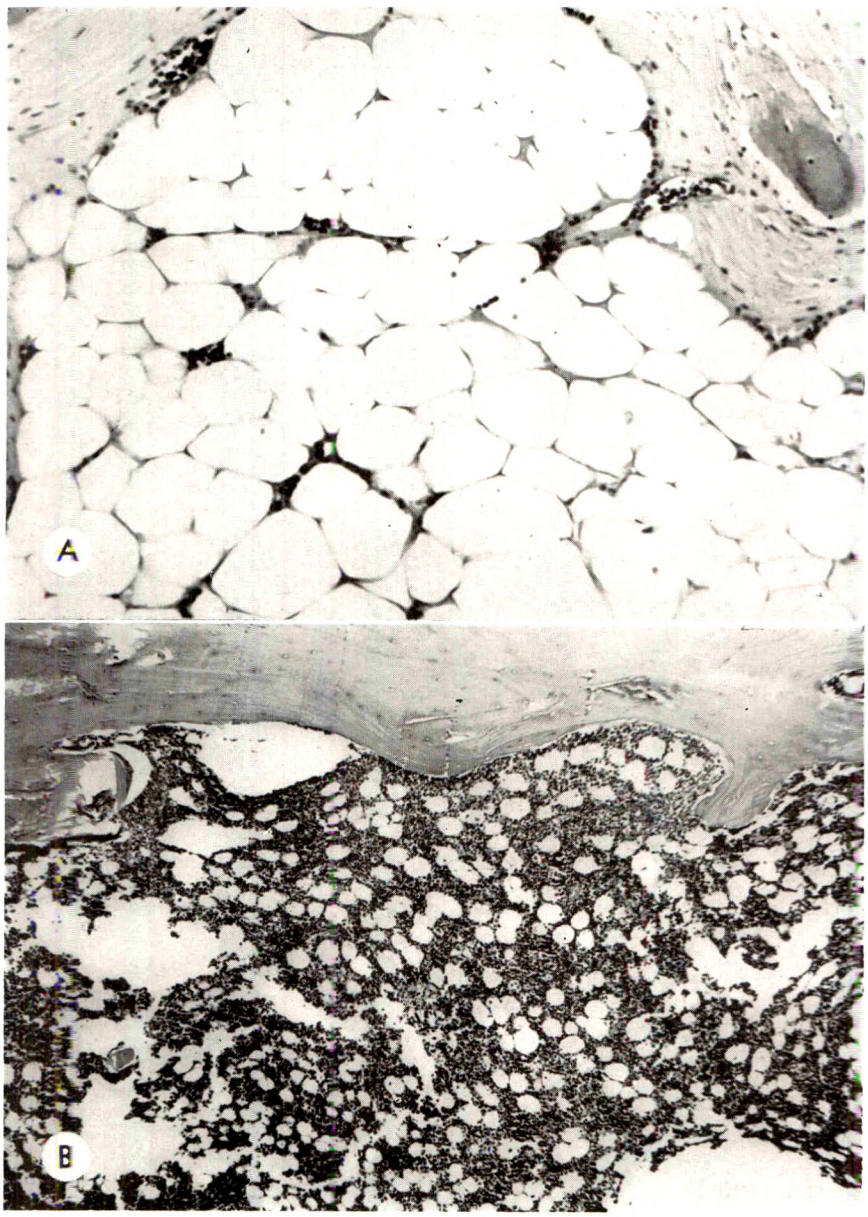


FIG. 9. (*A*) Photomicrograph of sternal marrow taken from irradiated field six months post irradiation (3,600 r). A focal area of hypocellular marrow is present. Hematoxylin-eosin stain ×196. (*B*) Photomicrograph of sternal marrow taken from area remote from field of irradiation six months post irradiation (3,600 r). Normal hematopoiesis is seen. Hematoxylin-eosin stain ×58.

sures between the intact arteries and the small intercoronary communicating vessels in the area immediately adjacent to the ischemic myocardium. Their data suggested that such preformed intercoronary anastomotic connections were available in the majority of dogs studied. Bellman and Frank[2] state that though this system of communicating vessels is present, there is normally no substantial flow through these collateral channels because of their high resistance to blood flow. They also state that no substantial flow through these channels is to be expected immediately following coronary occlusion despite the maximum pressure gradient resulting from

the occlusion. Survival then apparently depends upon the adequate functioning of this preformed intercoronary bed at the time of occlusion. It is believed that dilatation of any of these intercoronary vascular channels (terminal arterioles, intercoronary arterial vessels, venules, capillary bed) must necessarily be accompanied by similar dilatation of all the rest.[1] We postulate that successive small doses of radiation produce dilatation of the existing myocardial capillaries and precapillary arterioles and thus account for the demonstrated increase in survival rate and the evidence of increased blood flow. There was no evidence of formation of granulation tissue with subsequent new vessel formation at the doses of radiation administered.

In the present study it was seen that when the anterior descending coronary artery is ligated in a nonirradiated dog, a large area of myocardium, corresponding to the distribution of the ligated vessel, is deprived of the normal inflow of blood. All blood to this area must now enter in a retrograde fashion from branches of the left circumflex and right coronary arteries adjacent to the area of infarction. That this intercoronary anastomotic supply is functionally inadequate in the normal dog is demonstrated by the injection studies which show a bare area, devoid of barium or plastic, corresponding to the distribution of the anterior descending coronary artery. There were few, if any, intercoronary anastomotic connections open to permit the filling of this area in a retrograde fashion. Analysis, however, of the irradiated animals reveals the presence of functioning anastomotic channels through which barium and plastic flow in a retrograde fashion. The region of the myocardium supplied by the ligated vessel was thus filled and the bare area seen in the nonirradiated animals was not seen to the same extent. Irradiated hearts appeared in many cases to be completely vascular, despite the fact that the arterial inflow of a major vessel had been completely occluded.

Lumb and co-workers[6] have reported that following ligation of the anterior branch of the left coronary artery "the surviving animals had infarction of the entire thickness of the anterior wall of the left ventricle distal to the ligature." The nonirradiated dogs in our study exhibited this finding. However, of great interest is the fact that the irradiated hearts did not exhibit this "through and through" infarction, but contained a spared area of normal muscle in the subepicardium overlying the area of infarction. The presence of this extra area of normal muscle is important as regards the heart's ability to recover from the infarction. There is now a new dimension from which the reparative processes can occur. This also acts to accelerate the healing process. In the control dogs the necrotic area of infarction remained longer without being replaced by granulation tissue, and calcium was deposited in the necrotic muscle. In the faster healing irradiated dogs, there was much less opportunity for calcium deposition as the necrotic muscle fibers were absorbed by the healing process.

In the present study the cardiac irradiation was carried out directly through both lung fields. In the human application, an anterior chest field avoiding lung tissue could be used and thus the pleural effect noted at the higher radiation doses could be prevented.

SUMMARY AND CONCLUSIONS

1. Ligation of the anterior descending coronary artery has been performed on 66 dogs following varying doses of cardiac irradiation at varying intervals of time. A pathologic analysis of the hearts by means of injection and corrosion studies, and gross and microscopic examination has been carried out. Thirty control dogs, similarly ligated but not irradiated, were studied in the same manner. Nineteen irradiated animals, dying at varying intervals during and after radiation therapy (but prior to coronary ligation), were also studied.

2. The irradiated animals presented functioning intercoronary anastomotic chan-

nels at the time of coronary ligation.

3. A spared area of normal muscle was seen in the subepicardium overlying the area of infarction in the irradiated hearts. This finding was not observed in the nonirradiated control hearts.

4. Irradiated hearts healed faster than equivalent control hearts following myocardial infarction, as healing could occur from the spared area of normal muscle.

5. The effects of varying doses of cardiac irradiation upon the heart, lungs, bone marrow, hemogram and mediastinal tissues have been studied up to one year following irradiation. Evidence of focal radiation induced pleural and marrow changes directly under the field of irradiation was observed at some doses. The significance of these findings is discussed.

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THE USE OF TRIMETHOBENZAMIDE (TIGAN) FOR THE TREATMENT OF RADIATION INDUCED NAUSEA AND EMESIS*

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NAUSEA and vomiting are frequent complications of radiation therapy. There is no universally accepted explanation of their etiology. The possible factors mentioned in the literature include: (a) toxic cellular disintegration products;[2] (b) destruction of intestinal mucosa following abdominal irradiation;[24] (c) choline poisoning;[15] (d) general debility and cachexia in a patient with advanced cancer;[21] (e) vitamin deficiency;[11] (f) histamine release;[5,6,12] (g) increased capillary permeability and a shock-like syndrome;[10] (h) chloride depletion;[13] and (i) psychic factors.[9]

It is not surprising that, with such variation in the suggested etiology, the recommended therapeutic measures are also extremely varied. Thus, in the past, good results have been claimed following the administration of: (a) sodium chloride;[21] (b) various members of the vitamin B complex,[8,16] especially pyridoxine;[18,22] (c) vitamin C;[6] (d) parenteral liver therapy;[4,26] (e) antihistaminics such as benadryl;[12] and (f) hormones, *e.g.*, desoxycorticosterone acetate[5] and ACTH.[23]

In recent years, much attention has been focused on drugs with a specific antiemetic action. Cyclizine (marezine)[22] and dimenhydrinate (dramamine)[19] and also many members of the phenothiazine group of drugs have been investigated. Among the latter, chlorpromazine (thorazine),[14] perphenazine (trilafon),[3] prochlorperazine (compazine)[20] and mepazine (pacatal)[22] have been studied. Drowsiness is a frequent side effect of all of these drugs. With some of the phenothiazine derivatives, especially thorazine, more serious side effects, such as hypotension and jaundice,[7] have been reported. The drowsiness that may accompany the use of these agents is especially undesirable when radiation therapy is carried out on outpatients.

Because of the possible undesirable side effects of the phenothiazine derivatives, it seemed worthwhile to investigate the therapeutic efficacy, in radiation induced nausea and emesis, of trimethobenzamide (tigan), a recently introduced antiemetic, chemically unrelated to the phenothiazines.

MATERIAL AND METHOD

The material for this study was selected from 276 consecutive patients undergoing cobalt 60 teleradiation therapy with skin doses ranging from 1,250–2,000 r per week and with treatment portals ranging from 5×5 to 12×20 cm. In an effort to eliminate some of the psychologic factors, no patient was told that nausea and vomiting might accompany the treatment. Only those patients who did not have nausea or vomiting prior to therapy and who complained spontaneously of this complication within the first ten days of treatment were included in the investigation. There were 54 such patients and these were arbitrarily divided into two groups. The 31 patients in the first group received 200 mg. of tigan four times daily, and the 23 patients in the second group received a placebo, designated "tigan X," which was identical in appearance with tigan. The technician allocating the drugs did not know which was the active drug and which the inert placebo.

Evaluation of the results was made forty-eight hours after the institution of medication by one of us (J.A.B.), who sim-

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ilarly did not know whether the antiemetic or the placebo had been administered to the patient. The identity of the medication was revealed only after the therapeutic results had been evaluated in all patients.

The intensity of the symptoms was graded as: (a) severe (severe nausea and frequent vomiting); (b) moderate (infrequent vomiting and/or moderate to severe nausea); and (c) mild (little nausea and no vomiting). For purposes of evaluation, the patients in both the tigan and placebo groups were divided according to the intensity of their symptoms into 3 subgroups each, corresponding to the response to treatment which was graded as follows: (a) complete; (b) partial; and (c) no relief.

RESULTS

As mentioned above, only 54 of the 276 patients (20 per cent) complained of vomiting and/or nausea within ten days of the commencement of the radiation therapy. It can be seen in Table I that the incidence of nausea and vomiting varied with the area irradiated. It was highest (38 per cent) after irradiation of the abdomen, less (22 per cent) after irradiation of the thorax, and least (5 per cent) after treatment of other parts of the body.

As is obvious from Table II, which shows the effectiveness of treatment, tigan produced some degree of relief in 80.6 per cent of the patients and failed to do so in 19.4 per cent. Contrariwise, placebo medication was helpful in 60.8 per cent of the cases and ineffective in 39.2 per cent. Of the 4 patients in the subgroup with severe symptoms who received tigan, 2 derived partial relief and 2 were not benefited. On the other hand, none of the 3 patients in the corresponding subgroup who were given the placebo showed any improvement. Furthermore, of the 21 patients with

TABLE I

INCIDENCE OF NAUSEA AND/OR VOMITING AFTER COBALT 60 TELETHERAPY

Area Irradiated	No. of Patients Irradiated	Incidence of Nausea and/or Vomiting (First Ten Days of Treatment)				
		Site of Lesion	Tigan Group	Tigan X (Placebo) Group	Total No. of Patients	Per Cent
Abdomen	53	Adrenal gland	0	1	20	38
		Bladder	2	3		
		Cervix	2	2		
		Kidney	1	1		
		Lumbar spine	1	1		
		Mesenteric lymph nodes	1	0		
		Ovary	3	1		
		Stomach	1	0		
Thorax	139	Breast	11	9	30	22
		Esophagus	2	0		
		Lung	4	3		
		Mediastinal lymph nodes	1	0		
Head Neck Extremities	84	Brain	0	1	4	5
		Epiglottis	0	1		
		Maxilla	1	0		
		Tongue	1	0		
Total	276		31	23	54	20

TABLE II

EFFECTIVENESS OF ANTIEMETIC TREATMENT

Intensity of Symptoms	Tigan						Tigan X (Placebo)					
	No. of Patients	Complete Relief		Partial Relief		No Relief		No. of Patients	Complete Relief		Partial Relief		No Relief	
		No.	Per cent	No.	Per cent	No.	Per cent		No.	Per cent	No.	Per cent	No.	Per cent
Severe	4	0	00	2	50	2	50	3	0	00	0	00	3	100
Moderate	21	12	57	6	29	3	14	12	1	08	7	59	4	33
Mild	6	5	83	0	00	1	17	8	6	75	0	00	2	25
Total	31	17	54.8	8	25.8	6	19.4	23	7	30.4	7	30.4	9	39.2

moderate symptoms who received tigan, 12, or 57 per cent, derived complete relief and only 3, or 14 per cent, were not benefited, but, of the 12 patients in the corresponding subgroup who were given placebo medication, only 1 patient, or 8 per cent, experienced complete relief and 4 cases, or 33 per cent, were not benefited. In the subgroups with mild symptoms the results with tigan were only insignificantly superior to those with placebo medication.

No side effects attributable to tigan were observed in this series.

DISCUSSION

It is evident, both from the results of this investigation and from the reports of other workers,[19,22] that teleradiation applied to the abdomen produced more nausea and vomiting than that encountered after irradiation of other regions. Furthermore, the nausea and vomiting were more severe and refractory to treatment after irradiation of this area. Similarly, the incidence and severity of symptoms appeared to be greater after long-term than after short-term therapy.[19]

The therapeutic efficacy of such variable measures as those summarized earlier in this paper suggests the importance of psychologic factors in radiation-induced nausea and vomiting. This is confirmed by the number of placebo reactors seen both in this and other series. For example, Stoll[22] reported 53 to 75 per cent relief with placebos. Consequently, when assessing the therapeutic value of different drugs, it is necessary to consider not only the degree of relief obtained from the drug and from a placebo, but also the site irradiated, the amount of radiation given, and the severity of the initial symptoms.

Solan[20] compared the antiemetic effect of compazine, pyridoxine and a placebo in 45 patients. He found that 16 out of 16, 11 out of 14 and 9 out of 15 patients obtained some degree of relief after compazine, pyridoxine or a placebo, respectively. Unfortunately, no information was given regarding the site and dose of irradiation or the intensity of the initial symptoms. Marks[14] reported good results in 84 out of 85 patients with thorazine, but control studies with a placebo were not included in this investigation. Where larger doses (50 mg.) of thorazine were given intramuscularly, drowsiness occurred in some patients.

Dickson[3] obtained excellent results with trilafon in a small number of cases. However, here again no information was given regarding site or dose of irradiation or severity of symptoms, and no controls were used.

The results reported with pyridoxine have been conflicting. In Shorvon's[18] series, without placebo controls, 90 per cent improvement was reported. In a study with

placebo controls, Stoll[22] reported 54 to 60 per cent relief with pyridoxine, but he also found improvement in 53 to 75 per cent after a placebo. Silverman *et al.*[19] found pyridoxine or a mixture of pyridoxine and dramamine to be no more effective than a placebo.

Stoll[22] obtained 55, 76 and 77 per cent relief with marezine, thorazine and pacatal, respectively, when the site of irradiation was below the diaphragm. Although no results with placebos are given for this group, the over-all relief after placebos, reported in the same paper, was 54 to 60 per cent. Stoll considered pacatal to be the most satisfactory of these drugs. Side effects, in this investigation, were limited to a few cases of drowsiness after thorazine.

If the cases with severe and moderate symptoms in this study are combined, 20 of 25 patients who received tigan and 8 of 15 patients who were given the placebo derived some degree of relief. These figures (80 per cent for tigan and 53 per cent for the placebo) are similar to those quoted for pacatal and a placebo.[22] While tigan failed to give complete relief in any case with very severe symptoms, it did give partial relief in 50 per cent of such cases. On the other hand, placebo medication consistently failed to give any relief in this type of case. More than one half of the patients with moderate symptoms were completely relieved with tigan, but only 1 of 12 patients who received placebo medication in the corresponding subgroup became asymptomatic. Since the degree of relief with pacatal is not mentioned in Stoll's[22] study, a comparison of his results and ours is not too meaningful.

The clinical impression of the radiologists (J.A.B. and C.R.P.) participating in this study was that tigan was as good, or better, than the other drugs (pyridoxine, compazine, etc.) they had previously used for the treatment of radiation induced nausea and emesis. The lack of side effects from tigan was greatly appreciated by patients and radiotherapists alike.

In another study,[25] 200 mg. tigan, administered intramuscularly 3 times at three hour intervals after surgery, was only moderately effective against postoperative nausea and vomiting, as compared with placebo injections. In contrast, Adriani *et al.*[1] reported that 50 mg. of tigan administered intravenously was 100 per cent effective in the treatment of severe postoperative nausea and emesis. Considerably larger doses (200 mg.) were also used without ill effects for the same purpose by other investigators.[17] In view of these findings, an investigation of the efficacy of tigan given intravenously for the treatment of radiation induced nausea and emesis will be undertaken.

SUMMARY

1. Of 276 consecutive patients treated with cobalt 60 teleradiation with skin doses ranging from 1,250 to 2,000 r per week, 54 complained spontaneously of emesis and/or nausea.

2. The incidence of vomiting and/or nausea was 38, 22 and 5 per cent following irradiation of the abdomen, thorax, and other parts of the body, respectively.

3. Of the 54 patients who developed vomiting and/or nausea, 31 received 200 mg. tigan by mouth four times daily, and 23 were given a placebo of identical appearance. The study was carried out with a double blind technique.

4. Tigan produced some degree of relief in 80.6 per cent of the patients and was ineffective in 19.4 per cent. The corresponding figures for placebo medication were 60.8 per cent and 39.2 per cent.

5. In patients with severe symptoms, neither tigan nor the placebo was completely effective. Whereas tigan gave partial relief in 50 per cent of these cases, no relief at all was obtained with the placebo. In patients with moderate symptoms, tigan gave complete relief in 57 per cent and partial relief in 29 per cent. The placebo gave complete relief in only 8 per cent and partial relief in 59 per cent. In patients with mild symptoms, tigan and the placebo were almost equally effective.

6. No side effects were encountered with tigan.

7. It is concluded that tigan is an effective antiemetic in radiation induced nausea and vomiting.

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SPLENIC SCINTILLATION SCANNING*

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THE human spleen, roentgenologically homogeneous and lacking an opacifiable lumen, has not proved susceptible to satisfactory detailed roentgenologic study. It is chiefly by indirect evidence that splenic size and configuration may be evaluated. Opacification of the spleen with thorium dioxide has been virtually abandoned because of late sequelae. Splenoportography demonstrates the splenic veins but very little of the spleen itself. Colloidal gold-198 is concentrated by reticuloendothelial tissue wherever it lies and consequently has been used to demonstrate the spleen by scintillation scanning, but never without the unwanted accompanying image of the liver which itself traps much of the radioactive colloid. Further, the amount of gold-198 taken up by the normal spleen is said to be insufficient for clinical scintillation scanning.[1]

In a previous report[2] we have outlined the practicality of splenic scintillation scanning, without interference from hepatic radioactivity, by an atraumatic method which causes selective splenic uptake of radioactive red blood cells. We have since acquired experience with a second method which, like the first, is a means of modifying red blood cells so that they are trapped within the physiologic "filters" of the spleen and liver. Because its "filter" is the more efficient, the spleen acquires a considerably greater concentration of sequestered red blood cells than does the liver. We have reviewed both methods in detail elsewhere.[6] Briefly, normal red blood cells may be modified for trapping either by coating (*i.e.*, sensitizing) D-positive cells with high-titer human anti-D serum, or by heating the cells at 49.8°C. for 15 minutes (Fig. 1). Either isologous or compatible homologous red blood cells may be used. The heated cell technique, a clinically simple procedure, has significant advantages over the sensitization method. It is applicable to all subjects regardless of Rh genotype, affords less opportunity for contamination of red blood cells, requires only 30 minutes for preparation including

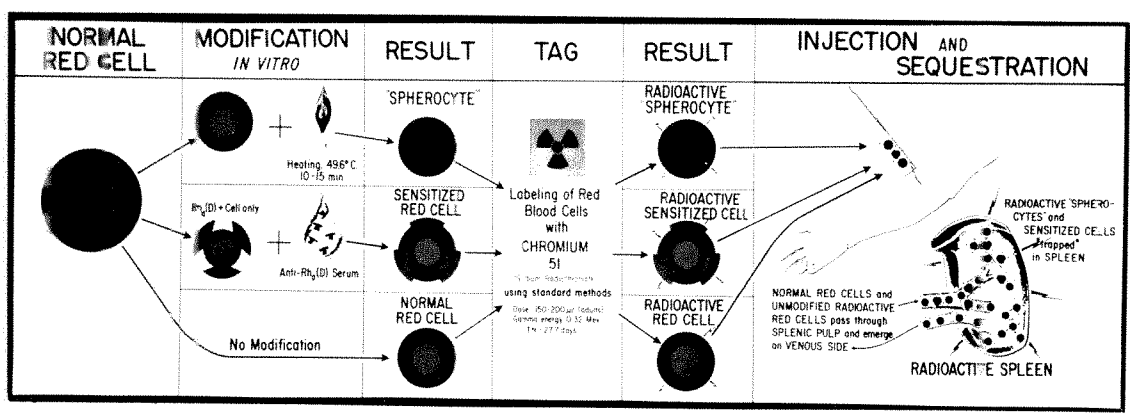


FIG. 1. Schematic illustration of methods of red blood cell preparation for splenic scintillation scanning.

* From the Department of Radiology, School of Medicine, University of North Carolina, Chapel Hill, North Carolina. This investigation was supported by U. S. Public Health Service Grant Number A-1996 (C1).
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† Present address: 141 Central Avenue, Montclair, New Jersey.

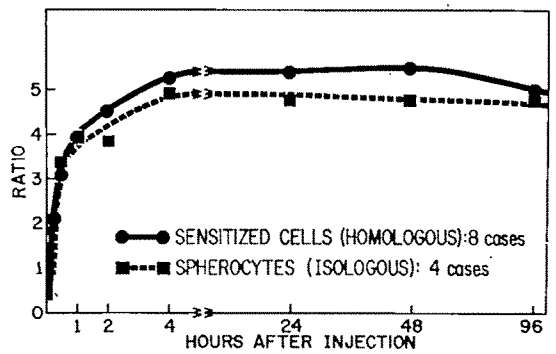


FIG. 2. Ratio of detectable splenic and hepatic radiation (S:L ratio) after administration of modified radioactive red blood cells.

addition of the chromium-51 label and results in a more rapid uptake of red blood cells by the spleen. Heating red blood cells in this manner increases their osmotic fragility, causing swelling of the cells and deformity into spheroidal forms which may in turn become microcytes by a type of fission.[2] These abnormal cells presumably become trapped in the splenic pulp after transfusion. The present study has shown the heated cell method to be applicable also to abnormal red blood cells from patients with sickle cell anemia and hereditary spherocytosis.

The relative splenic and hepatic uptake of transfused radioactive red blood cells is expressed as the spleen:liver ratio (S:L ratio) (Fig. 2). Scintillation probes are used to measure the detectable radiation in counts per minute at the skin over the spleen, liver and thigh. The thigh "count," an approximation of circulating or body background radioactivity, is subtracted from the gross spleen and liver "counts" to yield net values of the latter.

The rate of clearance of transfused radioactive red blood cells may be inferred from serial measurements of "body background" radiation, but quantitation of the red blood cell clearance (or survival) curve requires *in vitro* measurements of the amount of radioactivity per milliliter of red blood cells in serial samples (Fig. 3).

The scintillation scan may adequately be recorded by conventional printout on carbon-backed paper; however, we have preferred the photoscan technique because it allows contrast amplification, increases the appreciation of splenic configuration and permits later superimposition of the roentgenographic image of the spleen. The "dot" scan is useful as a visual monitor during the scanning process. In this investigation we employed a 2-inch scintillation crystal with cylindrical collimator, thus obtaining high sensitivity at the expense of relatively low resolution.

THE NORMAL SPLEEN

Our concept of the normal splenic scintiscan is based on experience with adult subjects without clinical or laboratory evidence of splenic disease (Table 1). Sensitized red blood cells were used in 8 cases, heated red blood cells in 4. The normal spleen and liver acquire radioactivity rapidly after transfusion. A greater concentration of

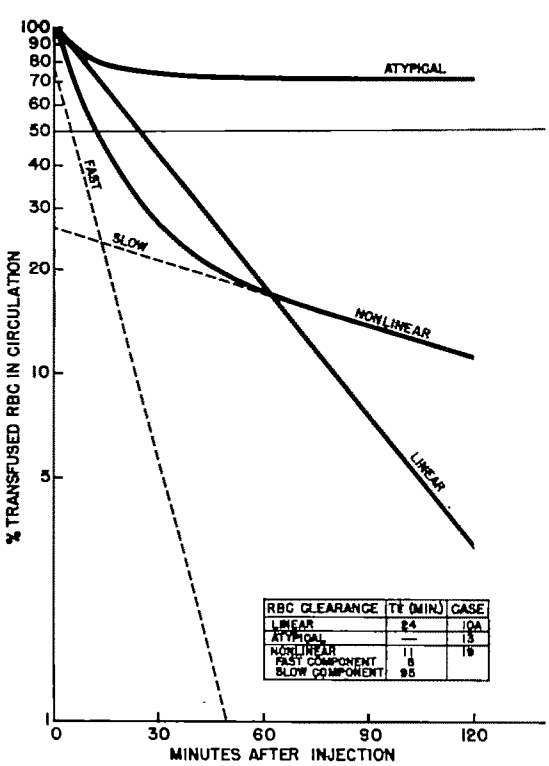


FIG. 3. Representative curves illustrating clearance of modified radioactive red blood cells from the circulation.

TABLE I

SELECTED DATA FROM CLINICAL STUDIES

Case, Age, Race, Sex	Disease Affecting Spleen	Dose Cr^{51} (μc)	Transfused Red Blood Cells					Length of Study (da.)	S:L Ratio at (hr.)	Area of Spleen (cm^2.)	Remarks
			Description*	Modified by	Half-Life (min.)	Clearance Curve	Reaction				
1. 57 CF	None	200	H D+	Serum	48	Linear	0	5	5.8:1 (24)	—	No scan (refused by patient)
2. 43 CF	None	200	H D+	Serum	98	Linear	0	19	5.6:1 (24)	70	
3. 54 CM	None	200	H D+	Serum	11	Nonlinear	0	56	1.9:1 (24)	—	No scan (atypical sequestration pattern)
4. 62 CM	None	200	H D+	Serum	47	Linear	0	70	6.3:1 (24)	80	
5. 26 CM	None	200	H D+	Serum	27	Linear	0	26	2.9:1 (24)	70	
6. 56 CM	None	200	H D+	Serum	24	Linear	0	2	5.6:1 (24)	60	
7a. 36 CM	None	150	H D+	Serum	49	Linear	0	33	4.6:1 (24)	60	Initial study
7b. 36 CM	None	150	I	Heat	30	Nonlinear	0	36	3.7:1 (24)	60	Repeat study at 7 mo.
8. 53 WM	None	150	H D+	Serum	50	Nonlinear	0	11	5.4:1(24)	60	
9. 48 WM	None	150	H D+	Serum	34	Linear	0	24	8.4:1 (24)	80	
10a. 55 CM	Myelofibrosis	250	I	Serum	24	Linear	0	11	?	160	Initial study. Recent Fe^{59}
10b. 55 CM	Myelofibrosis	150	I	Serum	—	—	0	2 hr.	5.5:1 (2)	120	Repeat study after roentgen therapy
11. 58 WF	Chronic Granulocytic Leukemia	150	I	Serum	—	—	0	2 hr.	8.8:1 (2)	220	Splenomegaly (clinically uncertain) proved by scan
12. 41 WF	1° Splenomegaly	150	I	Serum	21	Linear	0	4 hr.	8.5:1 (4)	180	Splenomegaly (clinically uncertain) proved by scan
13. 42 WM	Lymphosarcoma	200	I	Heat	?	Atypical	0	30 hr.	5.4:1 (24)	120	Insufficient heating. Only 29% of tagged RBC was cleared
14. 62 WM	Lymphoblastic Lymphoma	200	I	Heat	20	Nonlinear	0	55	7.2:1 (24)	80	Splenomegaly (clinically diagnosed) disproved by scan
15. 62 WM	Fatty Metamorphosis, Liver	150	I	Heat	?	Atypical	0	1	2.8:1 (24)	—	No scan. Insufficient heating. Only 20% of tagged RBC was cleared
16. 66 WF	"Thorotrast" Spleen	200	I	Heat	—	—	0	44	2.9:1 (24)	20	
17. 76 WM	Chronic Lymphocytic Leukemia	200	I	Heat	4.3	Nonlinear	0	2	8.3:1 (24)	160	
18. 27 WF	Hereditary Spherocytosis	150	I	Heat	—	—	0	1	2.7:1 (24)	110	Scan of resected spleen (340 gm.)
19. 66 WM	None	200	I	Heat	11	Nonlinear	0	25	5.7:1 (24)	60	
20. 80 CM	None	200	I	Heat	32	Nonlinear	0	25	5.0:1 (24)	40	
21. 66 CM	None	200	I	Heat	20	Nonlinear	0	25	4.3:1 (24)	50	
22. 28 WM	Laennec's Cirrhosis	185	I	Heat	—	—	0	42 hr.	19.0:1 (42)	100	
23. 32 WF	Chronic Granulocytic Leukemia	500	I	Heat	—	—	0	4 hr.	?	—	Recent Fe^{59}. Unsatisfactory scan
24. 40 WF	Laennec's Cirrhosis	200	I	Heat	—	—	0	4	22.0:1 (24)	120	
25. 22 WM	Lymphoblastic Leukemia	200	I	Heat	—	—	0	2	10.2:1 (17)	110	
26. 11 WF	Hereditary Spherocytosis	125	I	Heat	—	—	0	2	5.5:1 (24)	70	Scan of resected spleen (144 gm.)
27. 6 CM	Sickle Cell Anemia	100	I	Heat	—	—	0	3	10.8:1 (72)	60	
28. 28 CM	Sarcoidosis	145	I	Heat	—	—	0	2	8.5:1 (24)	180	
29. 30 CM	Sickle Cell Anemia	200	I	Heat			0	24	0.5:1 (24)	—	No scan (hypofunctioning spleen)
30. 54 WF	Laennec's Cirrhosis	200	I	Heat	—	—	0	22	18.9:1 (24)	110	

* H—homologous. I—Isologous.

radioactivity within the spleen becomes evident within 15 minutes. Reflecting this, the S:L ratio rises progressively to an average value of 5.3:1 (range 2.9–8.4:1) at four hours. At this time virtually all radioactive cells have been cleared from the circulation.

Maximum splenic radioactivity is reached between 24 and 48 hours after transfusion, and the average peak S:L ratio of 5.5:1 occurs at 48 hours. Thereafter physical decay plus exponential release of chromium from the spleen and liver cause a gradual steady decrement of radioactivity in these organs. Splenic scintillation scanning is best performed between the 4th and 48th post-transfusion hour, although it may be done at 2 hours or as late as 7–8 days.

The normal splenic photoscan (Fig. 4, *A* and *B*) reveals an area of nearly homogeneous density on the film; the density is maximal centrally. This area is defined by relatively sharp margins and its configuration fits the familiar roentgenologic depiction of the frontal projection of the spleen. The splenic image is variably rounded or ovoid but not circular. The splenic "notch" has not been demonstrated. The scanographic and roentgenographic images are virtually superimposable. On the posterior photoscan the normal spleen has an approximate mean area of 60 sq. cm. (range of 40 to 80 sq. cm.).

THE ABNORMAL SPLEEN

Nineteen studies have been performed in 18 patients with various diseases of the spleen. In each case the diagnosis was established definitively by appropriate methods (Table 1).

(a) *Hereditary Spherocytosis.* In 2 female patients hospitalized for hereditary spherocytosis, preoperative splenic scintiscans confirmed clinically noted splenomegaly and demonstrated homogeneous distribution of radioactivity in the enlarged spleens. Each patient was given isologous heated cells, augmenting the existing

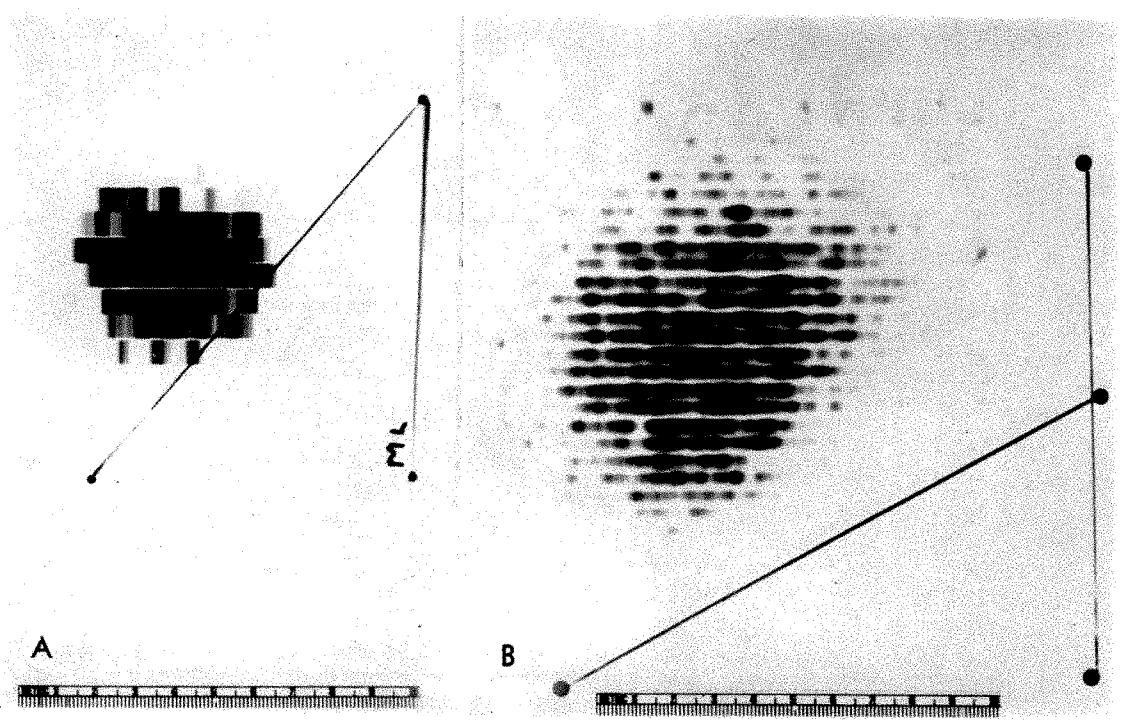


Fig. 4. (*A*) Lower (Case 20) and (*B*) upper (Case 9) limits of normal spleen size as demonstrated in the posterior photoscan.

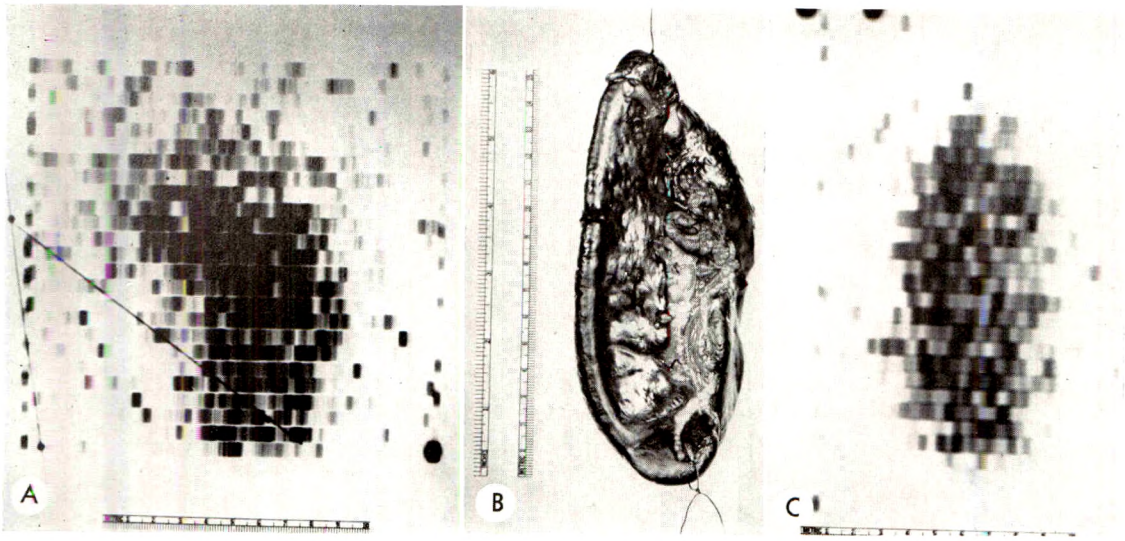


Fig. 5. Case 18. Hereditary spherocytosis. (*A*) *In vivo* photoscan shows splenomegaly. Compare with photograph (*B*) and photoscan (*C*) of resected spleen.

spherocytosis without macroscopic evidence of hemolysis. An eleven year old patient (Case 26) exhibited a 24 hour S:L ratio of 5.5:1, whereas a ratio of 2.7:1 was found in a twenty-seven year old patient (Case 18) (Fig. 5, *A*, *B* and *C*). Immediately after splenectomy the intact spleens were obtained for scintillation scanning. These scans demonstrated an essentially uniform dispersion of chromium-51 throughout the organ in each instance. Further, they confirmed the intrasplenic location of the chromium 51 and indicated the resolving capabilities of the cylindrical collimator.

(b) *Sickle Cell Anemia.* Two Negro males with sickle cell anemia, aged six years and thirty years, were studied with isologous heated cells. Limited study of the child (Case 27) using 100 μc of chromium-51 produced a 72-hour S:L ratio of 10.8:1, confirmed the presence of splenomegaly and showed uniform distribution of splenic radioactivity (Fig. 6). In the adult patient (Case 29), however, the S:L ratio at 24 hours was 0.5:1. Inversion of the ratio persisted without change during three and a half weeks of observation. Net splenic radioactivity remained low and no scan was performed. This patient's spleen was not palpable clinically nor visible roentgenologically. Measurement of body background levels suggested that the red blood cell clearance rate was unusually slow.

These patients represent widely separated clinical stages of sickle cell anemia, the adult patient having advanced well toward the condition of autosplenectomy.

(c) *Leukemia—Lymphoma.* Of 6 patients

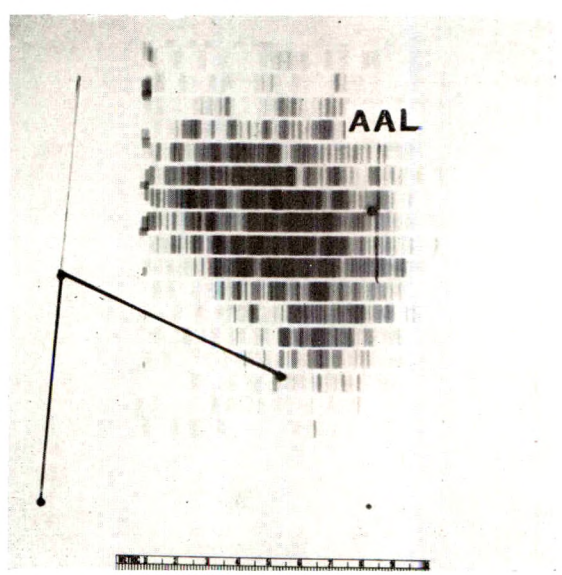


Fig. 6. Case 27. Sickle cell anemia with splenomegaly in a six year old child.

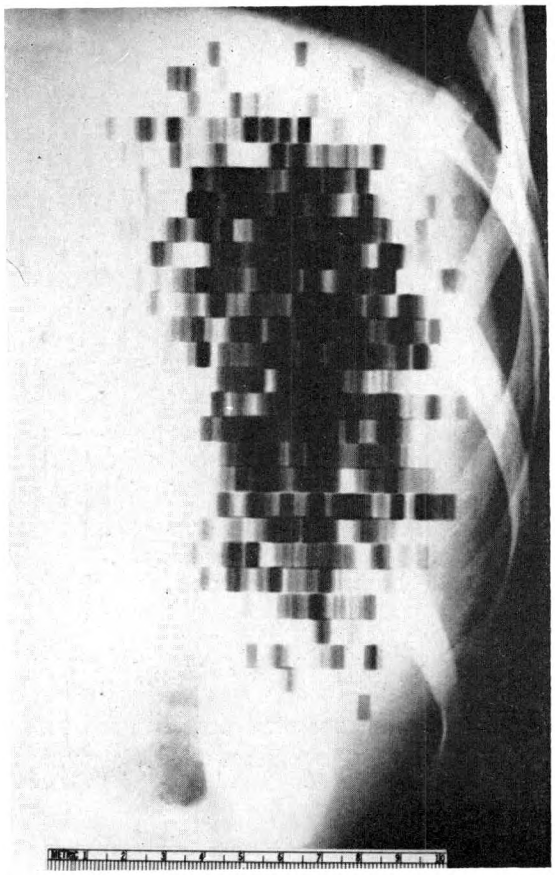


Fig. 7. Case 25. Acute lymphoblastic leukemia. Photoscan-radiograph shows predominantly central distribution of radioactivity in the enlarged spleen.

in this group, satisfactory splenic scans were obtained in 5, and splenomegaly was demonstrated in 4 (Fig. 7). The S:L ratios, measured at various intervals, ranged from 5.4 to 1 to 10.2 to 1. Both sensitized and heated cells were used. The enlarged spleens exhibited apparently homogeneous distribution of radioactivity throughout the parenchyma. In one patient (Case 14) a palpable left upper quadrant mass, thought clinically to be an enlarged spleen, was shown to be extrasplenic by the scan (Fig. 8, *A* and *B*). Conversely, in Case 11 a clinically atypical left-sided mass was proved to be the spleen.

Selective splenic uptake of isologous heated cells failed to occur in a thirty-two year old female (Case 23) with chronic granulocytic leukemia and massive hepatosplenomegaly. An unsatisfactory scan showed faint, equal density of each organ.

(d) *Hepatic Disease.* Of 4 patients in this group, failure to obtain a satisfactory splenic scan occurred in one (Case 15), a sixty-two year old male with fatty metamorphosis. In this case there was intentional inadequate heating of isologous red cells. That only a portion of these cells became morphologically abnormal is suggested by the atypical red blood cell clearance curve which leveled into a plateau at the 80 per cent level 10 minutes after transfusion. In 3 patients having Laennec's cirrhosis (Cases 22, 24, 30), very high S:L ratios occurred and satisfactory splenic scans were made. Each scan demonstrated splenomegaly with essentially homogeneous distribution of radioactivity. Lateral scans in 2 cases presented the splenic image in sagittal projection and demonstrated an anterior concavity (? liver impression) in one (Fig. 9, *A* and *B*).

(e) *Other Diseases.* Four patients with miscellaneous diseases are included in this group. Clinical splenomegaly was confirmed by splenic scan (Fig. 10, *A* and *B*) in an elderly male with myelofibrosis (Case 10). Shrinkage of the spleen was demonstrated by a repeat scan after completion of local roentgen ray therapy.

Splenomegaly with nonuniform distribution of radioactivity was demonstrated in a twenty-eight year old Negro male (Case 28) with systemic sarcoidosis (Fig. 11). A homogeneous splenic photoscan was obtained in a forty-one year old white female (Case 12) with slight splenomegaly of indeterminate etiology; clinically, the presence of splenic enlargement had been equivocal. In the final patient (Case 16), a sixty-six year old white female, thorium dioxide had been employed for carotid arteriography seven years earlier, and roentgenologically the spleen was shrunken and opacified. Diminution of splenic function was suggested by a 24 hour S:L ratio of 2.9:1, but a satisfactory photoscan was obtained. This demonstrated a splenic area

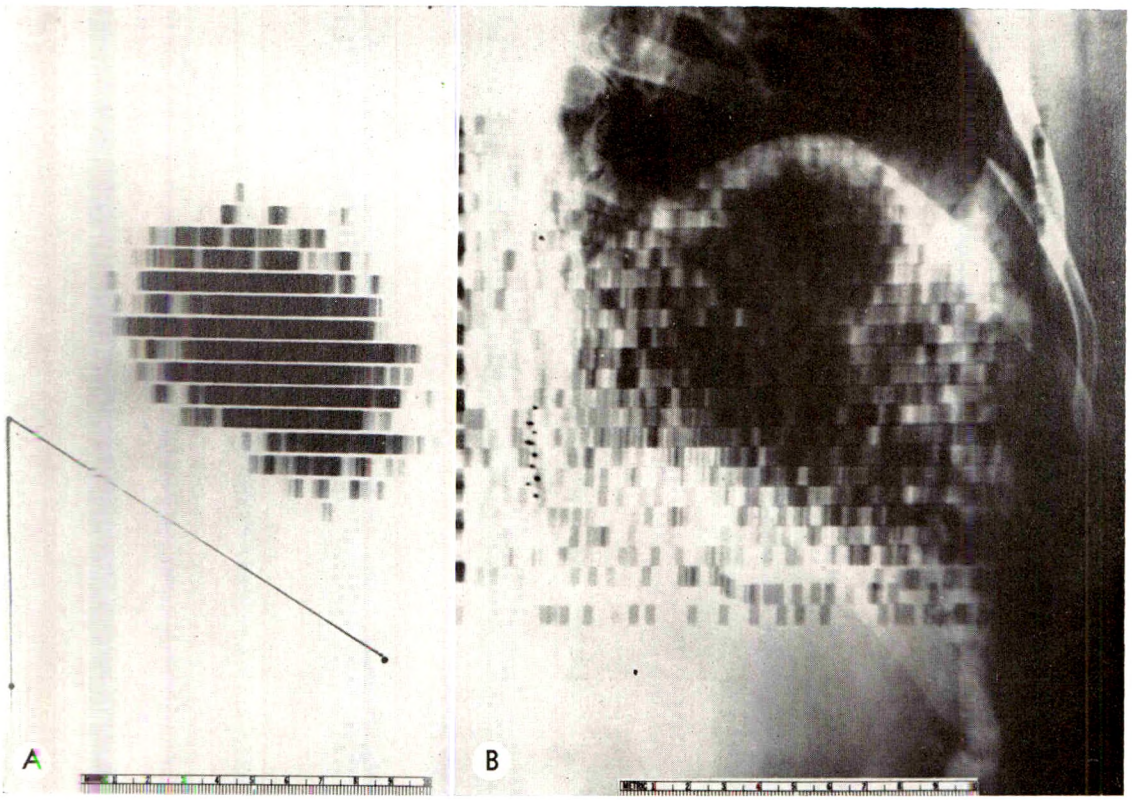


Fig. . Case 14. Lymphoblastic lymphoma. (*A*) Photoscan and (*B*) photoscan-radiograph. Clinically diagnosed splenomegaly was disproved by scan; left upper quadrant mass was extrasplenic.

of only 20 sq. cm. Of interest was the location of the splenic photoscan image *below* the opaque roentgenologic image on the combined photoscan-radiograph (Fig. 12, *A* and *B*). A conceivable explanation for this discrepancy is that an accessory spleen had formed after the thorotrast insult to the primary spleen and was the source of radioactivity.

HAZARDS

No untoward or undesirable reaction was observed in this investigation. The potential hematologic hazards are virtually negligible. Using ABO- and Rh-compatible red blood cells, the danger of inducing significant antibody formation is minimal. Nevertheless, it may be eliminated by using the patient's own cells. *In vivo* red blood cell coating by excess (unbound) anti-D serum in the transfused red blood cell suspension is preventable by washing the cells after sensitization. Even the remote possibility of hemolysis of all transfused blood should have no significant clinical effect since only 6 to 8 ml. of red blood cells are administered.

The amount of radiation delivered to the whole body, the liver and spleen, and the gonads depends on the variable factors of chromium-51 dosage, rapidity of red blood cell clearance, relative concentration of sequestered cells in the liver and spleen, the masses of these organs and their distance from the gonads.

Using reasonable assumptions based on data derived from this investigation, the calculated *total radiation doses* to various tissues after administration of 150 μc of chromium-51 bound to modified red blood cells are as follows: the *whole body* receives not more than 54 millirads; the *ovary* receives 63 millirads; the *testis* receives 18.5 millirads; the *liver* receives 319 millirads;

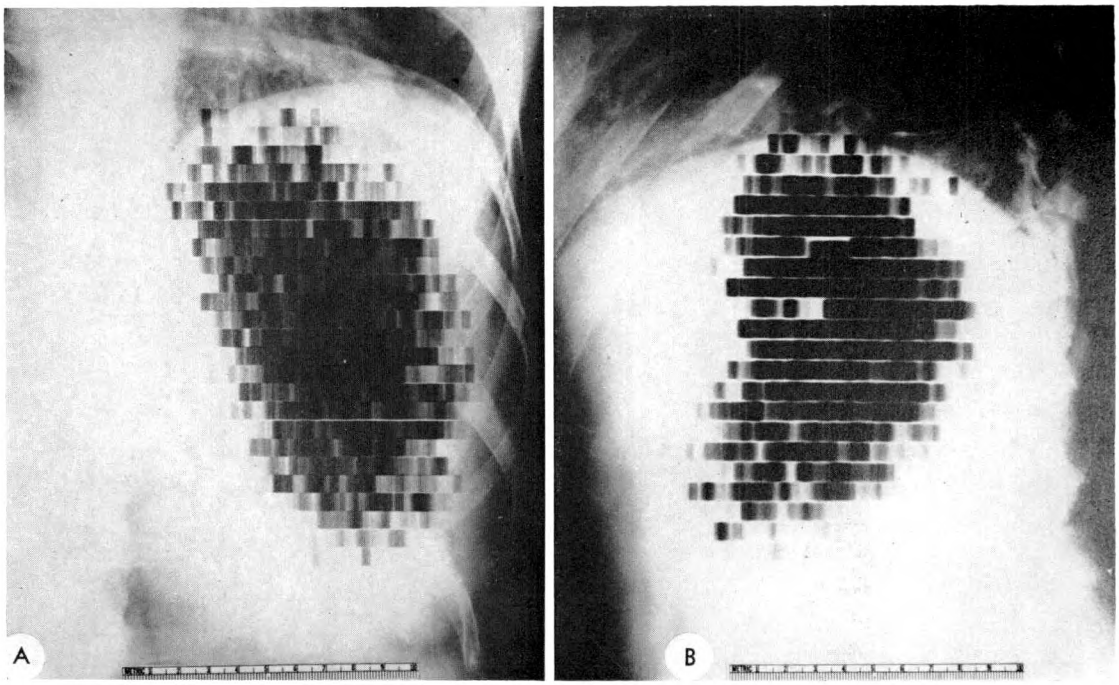


Fig. 9. Case 24. Laennec's cirrhosis with hepatosplenomegaly. (*A*) Frontal and (*B*) lateral photoscanradiographs reveal location of enlarged spleen and homogeneous distribution of radioactivity.

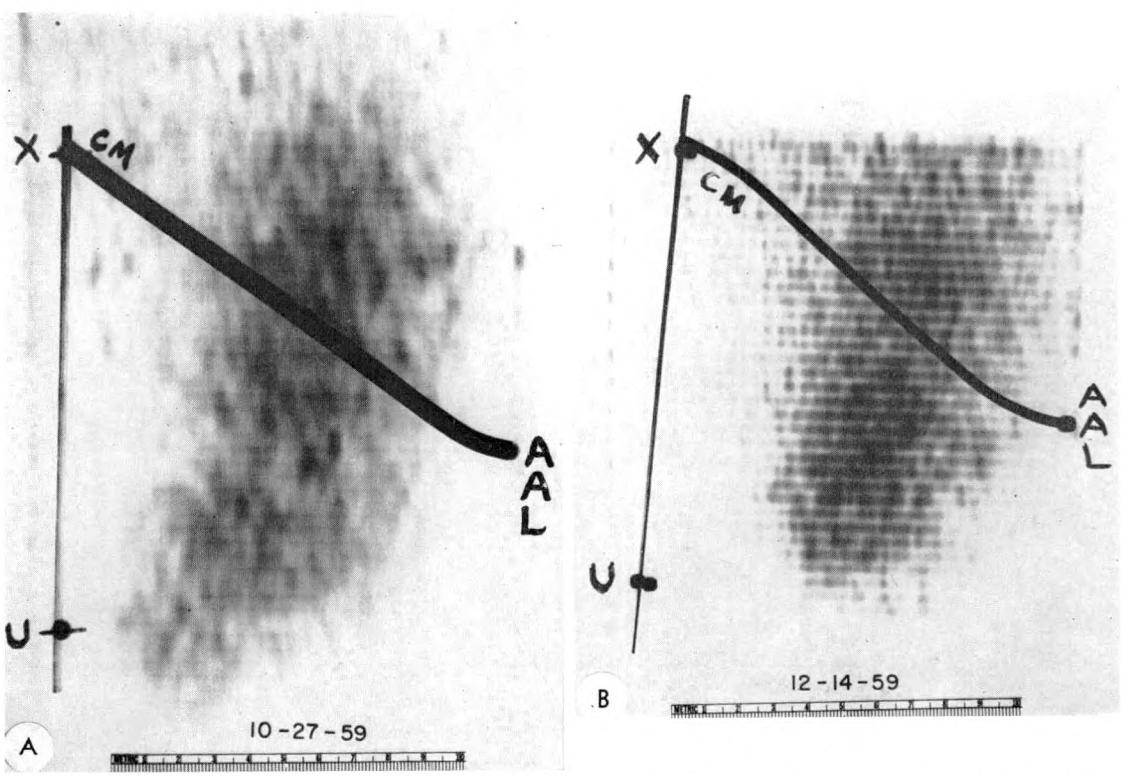


Fig. 10. Case 10. Myelofibrosis with marked splenomegaly. Anterior photoscans show (*A*) initial enlargement of spleen and (*B*) shrinkage of organ after roentgen irradiation.

and the *spleen* receives 10.7 rads.* The spleen, sequestering the majority of the radioactive red blood cells, acquires the greatest amount of radiation. The total splenic dose of 10.7 rads may perhaps be compared to the dose delivered to a 40 gm. thyroid gland taking up 9 μc of iodine-131 with an effective half-life of 5.5 days; under these conditions the thyroid gland receives a total dose of 19 rads.

DISCUSSION

On the basis of this investigation an assessment of the clinical value of splenic scintillation scanning can be made. The splenic scan objectively demonstrates the size, location and configuration of functioning splenic tissue. This delineation lacks the high resolution of which roentgenologic methods are capable, a disadvantage which is offset by the frequency with which a complete splenic image is seen. The splenic scan is valuable in the differential diagnosis of mass lesions of the left upper abdomen, as in Case 11 and 14, and permits a positive statement concerning the presence or absence of splenomegaly, as in Case 12. The splenic scan may permit identification of accessory splenic tissue; only further experience will clarify this possibility. This statement also applies to the use of red blood cell trapping for rapid localization of the small or slightly enlarged spleen prior to splenoportography.

Except for one patient with sarcoidosis, the available clinical material did not provide an opportunity to study discrete intrasplenic granulomata or other localized lesions; the volume of such lesions would largely determine whether they would be detected by a low-resolution collimator. However, focal intrasplenic lesions not only are uncommon but lack the significance of nonfunctioning hepatic and thyroidal nodules, the differential diagnosis of which frequently must include the possibility of neoplasia.

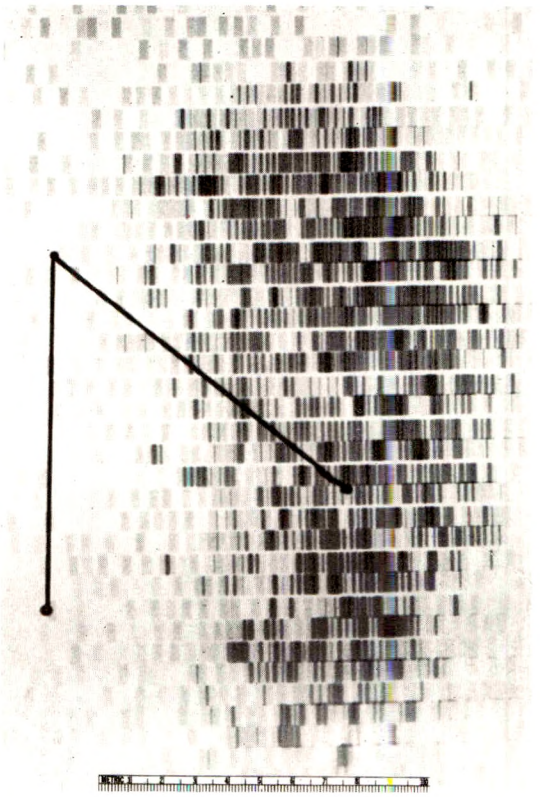


Fig. 11. Case 28. Sarcoidosis with splenomegaly. Nonhomogeneous distribution of radioactivity suggests partial replacement of functioning parenchyma by granulomata.

Two interrelated aspects of the splenic scanning procedure require additional investigation. A semilogarithmic plot (Fig. 3) of radioactive red blood cell clearance yields either a linear curve, reflecting the action of a single exponential function, or a nonlinear curve. Nonlinear curves can usually be resolved into two linear components of varying slope, indicative of two exponential processes acting simultaneously at different rates. We have observed linear and nonlinear curves in both normal subjects and patients with splenomegaly when sensitized cells were used, but have without exception seen only nonlinear curves when isologous heated cells were employed. Harris *et al.*[3] believe that the two components of the nonlinear clearance

* The assumptions employed in these calculations were: (1) 5/6 of the administered dose of 150 μc of chromium 51 enters the spleen and 1/6 enters the liver, with homogeneous distribution of the nuclide in each organ; (2) the effective half life of chromium 51 in the spleen and liver is 16.4 days and 21.8 days respectively; (3) the normal spleen and liver weigh 150 gm. and 1,700 gm. respectively their effective centers are 25 cm. apart; (4) the distance from spleen or liver to the ovary is 30 cm. and to the testis is 40 cm.

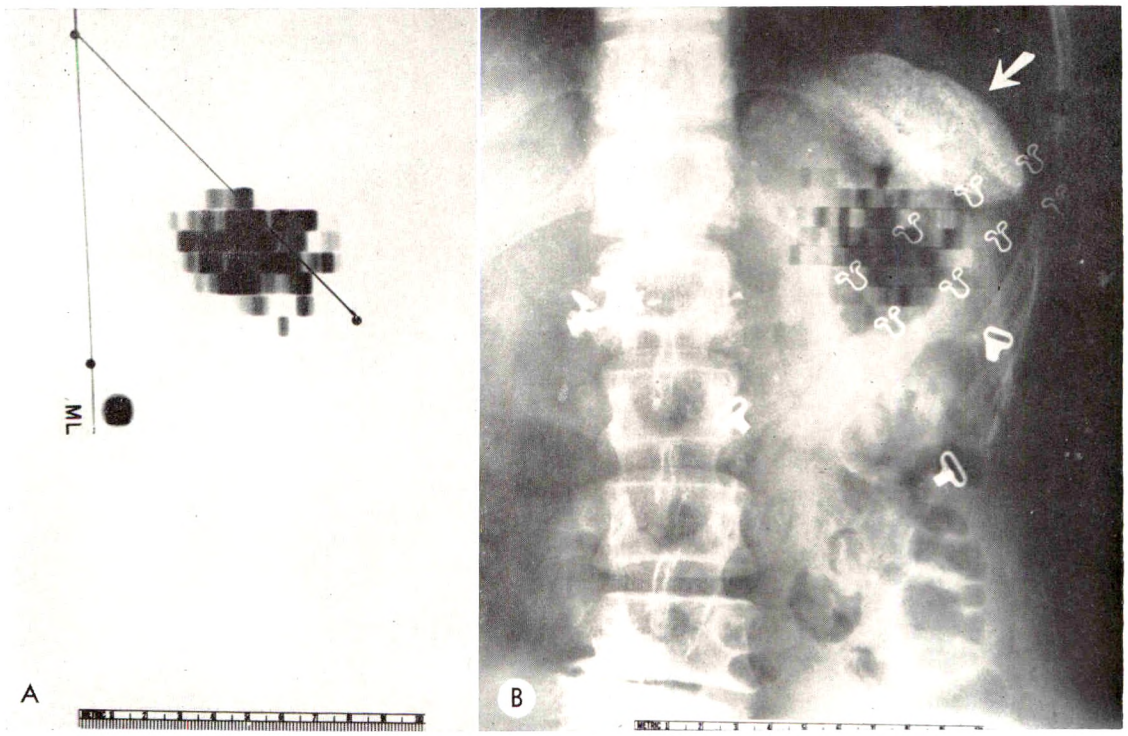


Fig. 12. Case 16. "Thorotrast spleen." (*A*) Note reduced area of splenic radioactivity and (*B*) its position below the contracted opaque spleen (arrow) on the photoscan-radiograph.

curve correspond to the rates of blood flow through two splenic "compartments," the closed or sinusoidal circulation and the open or pulp circulation. However, Weiss[7] has recently questioned the existence of an extrasinusoidal circulation in the human spleen. Hughes Jones *et al.*[4] postulate that the "fast" and "slow" components of the nonlinear clearance curve correspond respectively to intrahepatic and intrasplenic sequestration of red blood cells. Although the form, slope and half-survival time of the red blood cell clearance curve are determined in part by the type of red blood cell and its specific modification, these features presumably reflect as well the still-obscure processes of red blood cell removal and destruction.

The spleen:liver ratio is a measure of the relative activity of a physiologic process common to both organs. In this sense the ratio appears to have value as a clinical index of splenic and hepatic function. Unavoidable geometric errors affect any external determination of the concentration of radioactivity in two organs differing tenfold in mass; nevertheless the S:L ratio in our hands has been useful in measuring the splenic red blood cell trapping function. The upper limit of the range of the normal ratio probably does not exceed 10 to 1. We lack sufficient material to define the lower limit which may be 2 or 3 to 1. Of the diseases studied, only Laennec's cirrhosis with splenomegaly was associated with a significantly elevated S:L ratio. Our data suggest that the elevation resulted largely from decreased hepatic red blood cell sequestration, and raise the possibility that ratio measurement may have usefulness in the evaluation of cirrhosis and other hepatic diseases.

A feature of the S:L ratio observed in some cases was an often pronounced tendency toward fluctuation during the phase of red blood cell clearance. Whereas small changes may have been caused by such external factors as minor shifts in place-

ment of the scintillation probes, major fluctuations could reasonably be attributed only to real changes in the rates of splenic and hepatic sequestration. In Case 3, for example, it would be of interest to learn why an S:L ratio of 5.0:1 at 15 minutes had fallen to 1.9:1 at 24 hours. In this patient, who had no evidence by the usual criteria of splenic dysfunction, the clearance of the homologous sensitized red blood cells was nonlinear with a half-survival time of 11 minutes, an unusually low value. Future correlations of ratio measurements with red blood cell clearance curves may clarify the significance of these and similar findings.

SUMMARY AND CONCLUSIONS

These conclusions may be drawn from the present investigation of splenic scintillation scanning in a series of patients with normal or diseased spleens:

1. The splenic scintillation scan satisfactorily demonstrates the size, position and configuration of the functioning spleen without interference from hepatic radioactivity. It establishes the presence or absence of splenomegaly and thereby permits differentiation of mass lesions in the left upper abdominal area.

2. The technique of preparing red blood cells for the scanning procedure is clinically practical. There is no hematologic hazard to the recipient. The total radiation dose compares favorably to the amounts of radiation delivered in accepted clinical procedures using radioactive isotopes.

3. Further applications of splenic scintillation scanning may include the identification of accessory splenic tissue and the localization of the impalpable spleen for procedures requiring splenic puncture.

4. Measurement of the relative concentration of radioactivity in the spleen and liver has potential value as an index of a function common to these organs.

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EVALUATION OF LIVER FUNCTION WITH RADIOACTIVE IODIPAMIDE*

By JOHN R. McLAREN, M.D., JOHN T. GALAMBOS, M.D., *and* H. STEPHEN WEENS, M.D.
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SINCE Graham and Cole introduced the first roentgenographic contrast medium for evaluation of the biliary tract, a large number of oral compounds have been perfected. These have proved remarkably nontoxic and so efficient that roentgenography of the biliary tree is one of our most accurate examinations. The search for a compound which could be safely administered intravenously and which would be sufficiently concentrated by the liver to yield a satisfactory cholangiogram was less rewarding. Not until Langecker *et al.*[4] introduced a new chemical compound in 1953 was such an agent available. Soon thereafter Frommhold[1] and Hornykiewytsch and Stender[2] demonstrated the value of this compound for intravenous cholangiography. This compound has since been widely applied in medicine and in this country is more commonly known as Cholografin.

Frommhold noted that the urinary excretion of iodipamide was greater in patients with liver disease than in patients without liver disease. Numerous observations have been made as to a correlation between laboratory evidence of liver dysfunction and failure of opacification of the biliary tree on intravenous cholangiography. These experiences suggested that radioactive iodipamide, which can be easily assayed, might be used for a sensitive evaluation of liver function. A number of dogs was studied before and after liver damage was produced with either the inhalation of carbon tetrachloride or the surgical obstruction of the common bile ducts.[6] A striking decrease in the hepatic radioactive uptake was noted after the production of liver damage. The present study is of similar work on patients with and without liver disease and includes special applications of this technique.

PROCEDURE

Hospital patients were divided into two groups. One group consisted of patients with liver disease proved by clinical and laboratory means. A number of these had liver biopsies. The control group comprised patients admitted to the medical and surgical services without laboratory or clinical evidence of liver disease.

After an overnight fast, the patients were placed in the supine position and scintillation detectors were positioned over the heart and liver. The hepatic monitor was placed at the midclavicular line 3 cm. cephalad to the lower costal margin. Approximately 3 cm. clearance was permitted between the probe and the skin surface. The probe was a Nuclear Chicago model no. DS-5, serial no. 378, to which no additional collimation was added. An intravenous dose of 1 ml. of iodipamide per 40 pounds of body weight was administered. This contained approximately 15 μc of radioactivity. The change in radioactivity over the heart and liver was recorded by means of count rate meters and chart recorders for time intervals of approximately 10 to 15 minutes. An aliquot of blood was withdrawn after a 3 hour interval. Three and 24 hour urine and 48 hour stool collections were made.

Preliminary hepatic uptakes were obtained on patients to determine whether or not any correlation existed between the

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hepatic uptake of the radioactive iodipamide and subsequent opacification of the biliary tree on intravenous cholangiography.

RESULTS

The hepatic uptake curve of radioactivity can best be described by referring to Figure 1. Here the level of radioactivity represented by B is due to background radiation. Following the injection of radioactive iodipamide, there is a sharp rise in radioactivity and equilibrium is quickly reached at level E. The course that occurs from this point is the determining factor as to whether or not liver disease exists. Those patients without liver disease will show a definite upward trend, as indicated here. The results can be expressed as the per cent of increase or decrease of radioactivity from the equilibrium level by dividing the rise or fall (EC) by the equilibrium level (BE) and multiplying by 100. Those cases with borderline liver disease will have questionable concentration, whereas those with more marked liver disease will have a flat curve or actually show a decrease. The tracing in Figure 1 was made after a period of convalescence of proved hepatitis. An earlier tracing (Fig. 2) was made while the patient was in the hospital with hepatitis and shows a flat curve.

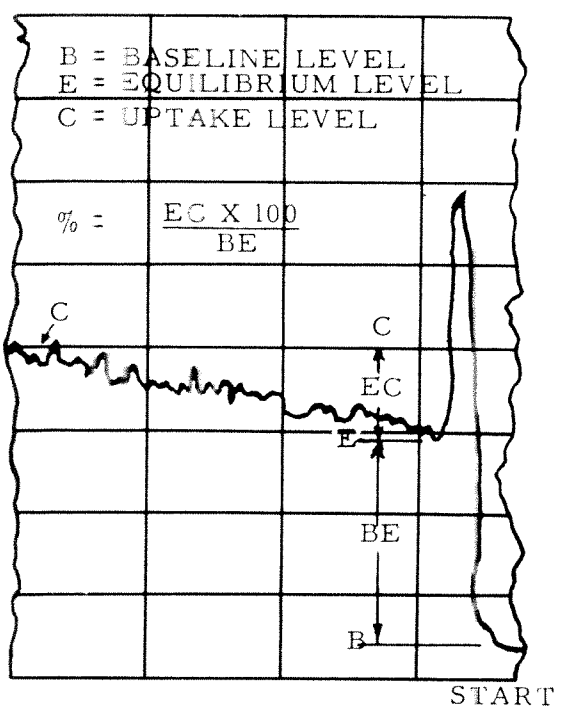


FIG. 1. The hepatic uptake of radioactive iodipamide in a patent after convalescence from hepatitis.

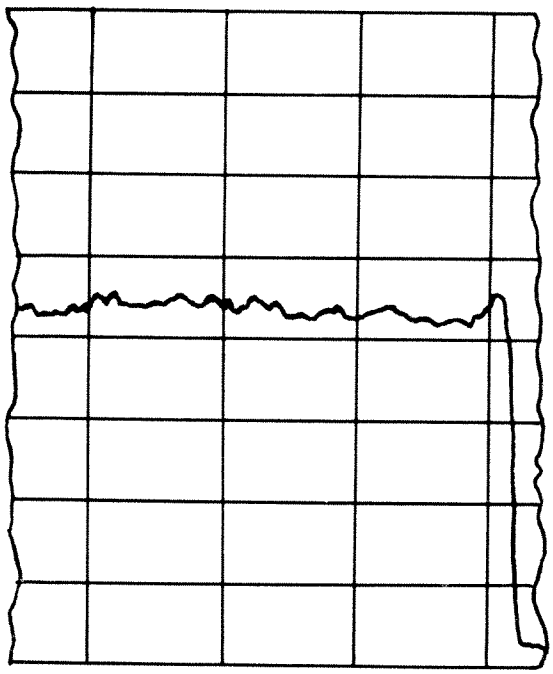


FIG. 2. The hepatic uptake of radioactive iodipamide in a patient with hepatitis (the same patient as in Figure 1).

A total of 36 patients with laboratory and clinical evidence of liver disease was included in this study. The average concentration of radioactivity above equilibrium levels was −3 per cent (±9). A total of 40 control patients was studied. The mean concentration of radioactivity by the liver above equilibrium levels in this group was +25 per cent (±12). Student's t value for this distribution is 4.4. The probability of this distribution being due to chance is less than 0.001.

The mean 3 hour urinary excretion for 10 controls was 2.5 per cent of the administered dose. The corresponding value for 15 patients with liver disease was 5.0 per cent. The 24 hour urinary excretion values were respectively 10.7 and 18.8 per cent. By use of the rank-sums test, the values for

TABLE I

RADIOACTIVE IODIPAMIDE DETERMINATIONS IN PATIENTS WITH AND WITHOUT LIVER DISEASE

Determination	Without Liver Disease		With Liver Disease		Probability of Chance Distribution
	Mean (per cent)	S.D.	Mean (per cent)	S.D.	
Hepatic Uptake	+25.0	±12.0	− 3.0	±9.0	0.001†
3 Hour Urine	+ 2.5	± 1.1	5.0	±3.0	0.10‡
24 Hour Urine	10.7	± 5.0	18.8	±8.6	0.001‡
3 Hour Blood*	9.2	± 5.8	13.0	±8.1	0.3‡
48 Hour Stools	32.0	±19.0	5.7	±6.7	0.01‡

* 1 liter of plasma.
† Determined by Student's test.
‡ Determined by rank-sums test.

3 hour excretion were shown to be significant at the 90 per cent level and for 24 hour excretion to the 99 per cent level.

The per cent of radioactivity remaining in the blood after 3 hours was calculated on the basis of one liter of plasma. The mean value for 19 controls was 9.2 (±5.8) per cent of administered dose as compared to 13.0 per cent (±8.1) for 21 patients with proved liver disease. These values were not significant when checked by the rank-sum test.

Stools of 6 patients without and 10 patients with liver disease were collected over a forty-eight hour period. The per cent of the administered radioactive iodipamide recovered in these collections was calculated. The mean values for the two groups respectively were 32 per cent (±19) and 5.7 per cent (±6.7). These results were significant to the 99 per cent level.

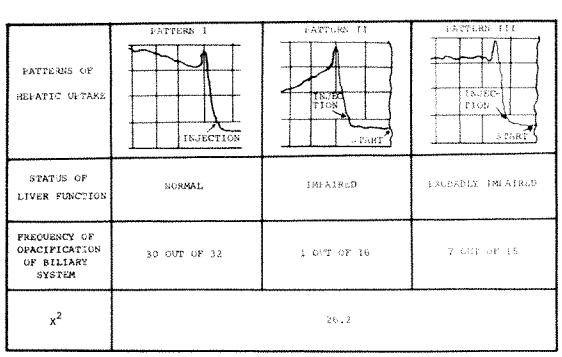


FIG. 3. The relationship between hepatic uptake patterns and frequency of opacification of the biliary system.

The various results given above are shown in Table I.

The hepatic uptake study also was performed on a total of 63 unselected patients for whom intravenous cholangiography had been requested. The technique was simplified in this group. A total of 2 ml. of iodipamide (1 ml. radioactive containing approximately 15 μc and 1 ml. test dose) was administered. The cardiac probe was not used.

The hepatic uptake curves can be divided into three basic patterns. The first of these shows definite hepatic concentration, the second shows a definite decrease in concentration in the liver, and the third is that in which the tracing is essentially flat (Fig. 3). Thirty-two patients showed Pattern I; in 30 of these the biliary tree was opacified on intravenous cholangiography. Pattern II was observed in 16 patients, and only 1 of these showed opacification of the biliary tract. Seven of 15 patients in the last category (Pattern III) showed opacification of the biliary tree on intravenous cholangiograms. Technical factors and habitus favoring good roentgenograms in this last group were important for biliary tract visualization. The chi-square value for the above distribution is 26.2, which is significant beyond the 99 per cent limits.

DISCUSSION

The course of the hepatic uptake curve after equilibrium is a balance between two parameters, namely, an increase of radio-

activity in the parenchyma and a decrease of radioactivity in the hepatic blood volume. A third factor, which is considered unlikely to affect the results because of the short time interval of the test, is the changing hepatic blood volume. Under these conditions curves with maximum or minimum points usually result. It is fortunate that the tracing obtained with this technique has a relatively flat maximum point and that a definite upward slope is obtained over a normal liver. The resultant curve is, therefore, easily interpreted. Although one can quantitate the results by calculating the per cent of increase or decrease in radioactivity from the equilibrium level, no complicated procedure is necessary for interpretation.

The uptake and excretion half times were determined by the method described by Lowenstein[5] for rose bengal. The uptake half time was approximately 30 minutes; the excretion half time, greater than 200 minutes. The long excretion time necessitates prolonged monitoring, which makes this procedure impractical for iodipamide.

It has been shown for radioactive rose bengal that, if the liver is monitored from the posterior aspect, contribution of radioactivity from the gallbladder will produce insignificant changes in the radioactivity monitored by the probe. Many of our patients were too ill or had too much ascites to lie in the prone position. For this reason we chose the supine position and monitored over the anterior aspect of the liver. The significant differences between the normal and abnormal groups justify the use of an anterior port. On a number of patients an additional probe was placed horizontally and the liver was monitored from a lateral aspect. These uptake curves were similar to those described in this paper.

We have previously shown that intravenous cholangiography can be of value in differentiating the entities producing the acute abdomen.[3] Unfortunately, approximately 40 per cent of patients presenting with an acute abdomen will fail to show opacification of the biliary tree and intravenous cholangiograms are indeterminate. This simple and rapid test, requiring little more time than the necessary sensitivity test for which it also serves, can be used to predetermine those patients in whom the biliary tree can be opacified. It should be pointed out, as indicated in an earlier paragraph of this presentation, that conventional laboratory studies likewise can be used. Unfortunately, the results of these tests are not always available when intravenous cholangiography is performed.

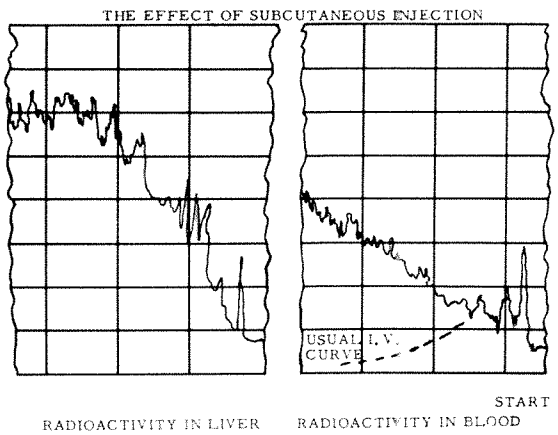


Fig. 4. Uptake curves after subcutaneous injection of radioactive iodipamide showing radioactivity in the liver (left) and radioactivity in the blood (right). (Reproduced by permission from *The Southern Medical Journal.*)

If a small quantity of iodipamide is infiltrated into the subcutaneous tissues, the hepatic tracing may be falsely read as showing good liver function. The curves after such an injection are shown in Figure 4. Usually the blood activity shows an exponential decay-type curve, as indicated by the dotted line in Figure 4. However, when significant amounts are given subcutaneously, the blood radioactivity slowly increases as the iodipamide is absorbed. In such cases the excellent concentration of radioactivity in the liver may indicate increasing radioactivity of the blood within the liver, not within the parenchyma. For this reason, the precordium was monitored with a second probe. However, this is not absolutely necessary since a sharp abrupt

rise on the hepatic tracing strongly favors an intravenous injection.

The number of cases included in the results of assaying biologic specimens is less than the number for hepatic uptakes. Some of the former were excluded because of contaminated or inadequately collected specimens.

Frommhold[1] indicated that the iodine was tightly bound to the iodipamide molecule and was not metabolized. Hence free iodine was not taken up by the thyroid gland. Monitoring of the thyroid gland subsequent to this test has failed to show appreciable radioactive uptake. However, in all probability, sufficient carrier iodipamide was present to block the uptake of I^{131} by the thyroid gland if any iodine were freed. Thyroid uptakes were performed on several patients without clinical evidence of thyroid disease and on whom hepatic uptakes of iodipamide had been done. The thyroid uptake values were in the myxedematous range, suggesting that sufficient iodine was released from iodipamide to block the thyroid gland.

Patients with congestive heart failure were excluded from this study because such patients failed to concentrate iodipamide. Further studies are in progress on the rate of reversibility of this defect following cardiac compensation. All 5 patients on whom multiple hepatic uptake tests have been performed have shown some increase in the uptake following cardiac compensation.

CONCLUSIONS

1. Statistically significant differences in the hepatic uptake of radioactive iodipamide were noted in patients with liver disease as compared to those without liver disease.

2. A definite upward slope of the normal hepatic uptake curve simplifies the interpretation of the test.

3. Nearly all patients showing a definite upward curve will subsequently show an opacified biliary tree on intravenous cholangiography.

4. Those patients who fail to show any concentration of radioactivity over the liver will rarely show subsequent opacification of the biliary tree on intravenous cholangiograms.

5. Approximately one-half of those patients in whom the hepatic uptake curve is flat or questionably upward in slope will show opacification of the biliary tree on intravenous cholangiography. In this group, habitus and technical factors for good roentgenography are of importance.

6. Significant differences between patients with and without liver disease were also noted in the excretion of radioactivity into urine and feces following the intravenous injection of radioactive iodipamide.

7. The clearance of radioactivity from the blood following the intravenous injection of radioactive iodipamide did not differ significantly in the two groups of patients.

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EDITORIALS

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The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine announces with deep regret the sudden death of Dr. Lawrence Reynolds on Thursday, August 17, 1961 in Detroit, Michigan.

Dr. Reynolds was Associate Editor of this Journal in 1928-1929 and its distinguished Editor since 1930 excepting the years of 1947 to 1949 during his tenure as President-Elect and President of the American Roentgen Ray Society.

DOSAGE LIMITATION IN THE COMBINED TREATMENT BY IRRADIATION AND SURGERY OF CARCINOMA OF THE UTERINE CERVIX

CONSIDERABLE initial enthusiasm has followed the revival of surgical techniques in the treatment of carcinoma of the uterine cervix. In the years since Wertheim's 1914 deploration: "It is a tragic fate being obliged to establish the fact that my life's work, the introduction of radical surgery in the treatment of carcinoma of the cervix has been unprofitable," radiotherapy has been acknowledged the more successful modality. Surgical recrudescence, foreshadowed in the development of the Taussig operation and the refinements of the Clark-Wertheim procedure and nurtured by better anesthesia, has been realized with the appearance of antibiotics and improved supportive care. Currently notable interest is evidenced in the feasibility of superimposing radical or quasi-radical operations upon high rad, large volume radiation dosages delivered to pelvic tissues.

Meaningful evaluation of normal pelvic visceral and supportive structure tolerances has been made by Wall *et al.*,[1] Frick *et al.*,[2] and Chau *et al.*[3] Their refreshing summations replace nonspecific roentgen administered tolerance gauging with details of time dose relationships, radium geometry and external radiation schedules. In the study of Wall *et al.*[1] severe complications appeared in 21 per cent of the patients receiving 4,000 r or more with external orthovoltage irradiation. Eight per cent developed major injury in those receiving 3,500 r to 4,000 r, and only a 2 per cent complication rate was observed in the 3,000 r to 3,500 r range. Doses in excess of 3,500 r added little to cure probability and greatly increased the risk of necrosis. Frick *et al.*[2] relate the difference in complication rates in those patients treated by radiotherapy to various dosage levels of external irradiation. Employing supervoltage techniques, injuries were significantly more common in patients given more than 4,000 r tumor dose. Dosages above 4,000 r to the pelvic wall have been abandoned by this group because of their hazardous consequences.

Chau *et al.*,[3] at the recent meeting of the American Radium Society, have discussed the complications appearing in 741 cases of cervical cancer. Patients receiving 4,000 r total pelvic irradiation exhibited freedom from persistent dysuria and bladder ulcer and almost no instances of proctitis or rectal ulcer were recorded. The incidence of sigmoiditis was practically nil at this dosage level. None of the patients in this group developed fistula or small bowel necrosis in the absence of an added surgical procedure. Chau *et al.* also concluded that higher dosage levels, provided no surgical procedure is added, are not conducive to excessive pelvic fibrosis or ureteral complications.

Several types of surgical procedures have been devised to meet various clinical situations. Brunschwig and Daniel[4] have described the most suitable operation when the rectum and bladder are uninvolved. "This is a radical panhysterectomy and pelvic node excision. The technique emphasizes complete node excision, including excision of the hypogastric artery and vein and denudation of the sciatic nerve roots in the posterior lateral pelvis." Complications peculiar to these surgical methods must be anticipated. Operative mortality has been effectively reduced; however, late postoperative complications remain the

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bête noire. Most important of these are ureterovaginal fistula, enteric fistula and bladder atony. Leg edema, wound infection, bowel stricture and adhesion produced intestinal obstruction are other adverse sequelae observed. In a group of early cases, cited by Frick *et al.*[2], undergoing radical hysterectomy and pelvic node dissection, major complications occurred in 18.4 per cent. Brunschwig and Daniel[4] performed this operation on 348 selected cases. Forty five urinary tract fistulae developed postoperatively. Many estimate that the incidence of ureterovaginal fistula alone will continue to occur in 10 per cent of the surgically treated cases.[2]

Combined aggressive surgical and radiotherapeutic measures expose the pelvic structures to the vicissitudes of both disciplines. Aside from the mathematical probability of increased complication rates, an additive factor appears inherent: blood supply already compromised by irradiation is further embarrassed by surgical intervention. Comparative studies in patients treated with radiation and those treated by combined approach reveal that the complications of both methods are potentiated when certain time dose radiation thresholds are exceeded. Frick *et al.*[2] found in three series of patients receiving at least 4,000 r that without added surgery the major complication rate was 5 per cent; with lymphadenectomy, the major morbidity incidence rose to 36 per cent, and in those subjected to radical hysterectomyand lymphadenectomy complications appeared in 20 per cent. In a parallel analysis in which patients received less than 4,000 r in the presence of superimposed surgery, complications were decreased by more than one third.

In the series of Chau *et al.*[3] small bowel necrosis, sigmoiditis and fistulae developed in 21.5 per cent of patients treated by radiation therapy and lymphadenectomy. Twenty three per cent in the group which had hysterectomy or exenteration with lymphadenectomy plus radiation therapy developed undesirable sequelae. They concluded that 4,000 rad whole pelvis irradiation is a safe technique even if lymphadenectomy and/or hysterectomy are added.

Gray and co-workers[5] regard the development of lymphocysts, occurring in 17 per cent of their cases, as a major problem in postirradiation lymphadenectomy. A lymphocyst is a collection of serous fluid which develops retroperitoneally in the denuded iliac vessel region. It appears that there is a correlation with the amount of tissue removed, and that a definitely higher number of lymphocysts is observed in persons receiving preliminary irradiation. This high incidence and the frequency of required secondary surgical procedures with prolonged convalescence create a prohibitive morbidity rate. Chau *et al.*[3] comment that these cysts can result in ureteral obstruction and effect vascular occlusion.

The prospect of increasing survival rates in carcinoma of the cervix is a constant lure to surgeons and radiotherapists. Some injuries are acceptable. Yet, a point of diminishing return is reached where complication yield precludes further treatment. Brunschwig and Daniel[4] have remarked that "Modern surgical attack in cancer of the cervix should for the present be confined to institutions with adequate equipment, whose personnel have the requisite surgical skill." Leucutia[6] in the Caldwell Lecture of 1960 reiterated, "The effect of reintroduction of radical surgery upon the over-all results appears to be statistically small and needs further investigative evaluation." Thus, the efficacy of treating carcinoma of the cervix with combined irradiation and radical surgery has not as yet emerged from the phase of experimental appraisal. However, when such a

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combined approach is contemplated, supplementary supervoltage external irradiation should not exceed 4,000 rads to the pelvic tissues. This is more than experimental data or work in progress; it is accumulated clinical fact. The clarion for higher survival rates from ever increasing radiation dosages and extensive surgery is muted by normal tissue intolerance.

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THE REGISTRY OF RADIOLOGIC PATHOLOGY

The American Registry of Pathology of the Armed Forces Institute of Pathology

IN 1947 the American College of Radiology, the American Roentgen Ray Society, and the Radiologic Society of North America jointly sponsored a Registry of Radiologic Pathology within the framework of the American Registry of Pathology. Outside of the academic family of medical schools, however, it would appear that relatively few physicians are aware of the purpose of the American Registry of Pathology, and that even fewer practicing radiologists know of the Registry of Radiologic Pathology. Perhaps the American Registry of Pathology can be of greatest service to those physicians outside the immediate academic family of medical schools. Since this group is relatively uninformed about the Registry, a brief historic background is indicated.

In 1862, nearly 100 years ago, the Armed Forces Institute of Pathology was founded. Originally known as the Army Medical Museum, it consisted of three dried and varnished specimens resting on a small shelf above the inkstand on the curator's desk. From this modest beginning, the Armed Forces Institute of Pathology today houses more than one million accessions, comprised of surgical biopsy specimens, complete autopsy data and specimens, and allied pathology material all filed for teaching, research and posterity. In 1946 the Army Medical Museum was renamed the Army Institute of Pathology. In 1949, following the unification of the armed services, the present designation, the Armed Forces Institute of Pathology of the Department of Defense, was adopted.

The Armed Forces Institute of Pathology has four major components: the department of pathology, the medical illustration service, the American registry of pathology, and the medical museum. Unknown to many civilian physicians is the consultation service for the diagnosis of pathologic tissue. The consultation service, established primarily for what is now the Department of Defense and other federal agencies, is also available to any civilian pathologist or other physician in need of a board of arbitration to help him arrive at a final pathologic diagnosis. It is obvious that such a service is probably of greatest value to those civilian physicians practicing outside of large academic institutions. Another function of the department of pathology is to prepare, or procure and duplicate, pathologic, photographic, and other educational material. This material is donated or loaned to other Federal medical services, museums, medical schools, scientific institutions, and to qualified persons connected with the medical, dental, or veterinary professions. Many civilian residents in the surgical and pathology specialties have availed themselves of these loan slides before taking their specialty board examinations.

The first of the American Registries of Pathology had its inception in 1922. In that year, Major George Russell Callender, curator of the Army Medical Museum, with the cooperation of the American Academy of Ophthalmology, organized a registry of ophthalmic pathology, where pathology relative to the eye could be collected and cases followed for study and research. In 1925 the second of the registries was organized, under the sponsorship of the American Association of Pathologists and Bacteriologists, to attempt to classify lymphatic tumors. Today there are 22 such registries all housed within the framework of the Armed Forces Institute of Pathology under the auspices of the National Research Council and each, except endocrine pathology, sponsored by a national medical, dental, or veterinary society. It is indeed fortunate that the farsighted thinking

of Dr. Callender has led to the housing in one repository of this tremendous wealth of pathologic material.

Criticism of the housing of the registries within an agency of the United States Government has been voiced by many academicians around the country. This criticism would sometimes appear to bear the implication of special pleading, since some of these specialists argue for the acquisition of a specific registry within their own academic institution. Obviously this treasury of information could easily be dispersed throughout dozens of deserving institutions—as could, indeed, the Library of Congress or the Smithsonian Institution, —thereby destroying its very reason for existence as a great corpus of information available to the United States Government and to all civilian physicians, dentists, and veterinarians.

In this period of history, when public funds are necessarily being directed to potentially destructive purposes in the interests of the nation's preservation, it is gratifying to see this great repository of scientific knowledge, built with public funds to amass knowledge for the alleviation of suffering, and to cure disease in generations to come.

In 1947 the fifteenth registry was organized, the Registry of Radiologic Pathology. At its inception, as is true of many new undertakings, there was little organization or purpose. However, in the intervening fourteen years, this registry has become one of the truly great study centers for correlation of disturbed morphology viewed radiologically and the gross and microscopic pathology of the tissues. There are now some 12,000 cases in this registry complete with history, reproductions of the roentgenograms, photographs of the gross pathology, and histologic sections.

The splendid organization of this registry is a labor of love of one man. Early in the life of the registry, the sponsoring societies realized that a consultant serving for one week each quarter was not enough, and that a part-time director in residence was necessary. Fortunately the right man was found. Colonel William L. Thompson, MC (Ret.), took on what was regarded as a part-time job and offered his services without remuneration. But the Colonel was not content to do a part-time job. Daily Colonel Thompson is at the Institute doing didactic teaching for four hours and spending the other four in accessioning new material and organizing the old. Not only does the Colonel impart a wealth of knowledge to the residents and fellows, but he succeeds in bestowing a spark of enthusiasm and joy for the practice of radiology to each man in turn. Nowhere, in the writer's opinion, is there so great an opportunity for a man nearing the end of his residency to pull all the loose ends together, and to correlate the various radiologic patterns of disturbed morphology in terms of gross pathology.

Dedicated men with Colonel Thompson's zeal and ability to teach are not common. It is hoped that the sponsoring organizations will actively look to the future for an able successor and a much more adequate remuneration than has been Colonel Thompson's lot in this important post.

In conclusion, the need for continually enriching the registry with new material is obvious. Such a registry should have within it the best that each teaching institution throughout the country possesses, both the esoteric and the routine. There is a great reluctance on the part of some specialists in various academic institutions to send cases for accession, on the grounds that the cases are lost for local reporting, and are eventually reported in the literature by the Armed Forces Institute of Pathology. This, of course, raises the question of whether medical writing should serve for personal aggrandizement, when the piecemeal publication of isolated cases obviously is less meaningful than comprehensive reporting by the Institute. For example, the study and reporting of pulmonary alveolar proteinosis might never

have been possible in a single institution. The Armed Forces Institute of Pathology, on its part, should be scrupulous in making full acknowledgment of the provenance of material it publishes.

It is hoped that more directors of departments of radiology throughout the country will avail themselves of the opportunity of sending their older residents to the Armed Forces Institute of Pathology for their pathology, and that more material, both esoteric and routine, will find its way to the registries.

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Philadelphia, 46, Pa.

BOOKS RECEIVED

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

BOOKS RECEIVED

THE USE OF ISOTOPES IN HAEMATOLOGY. By L. G. Lajtha, M.D., D.Phil., Member External Staff Medical Research Council, Radiobiology Laboratory, Department of Radiotherapy, Churchill Hospital, Oxford, England. Cloth. Price, $4.75. Pp. 83, with 27 illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

ONSETS, COMPLETIONS, AND SPANS OF THE OSSEOUS STAGE OF DEVELOPMENT IN REPRESENTATIVE BONE GROWTH CENTERS OF THE EXTREMITIES. By S. Idell Pyle, Harold C. Stuart, Joan Cornoni, and Robert B. Reed, Harvard University School of Public Health, 55 Shattuck Street, Boston 15, Massachusetts. Paper. Price, $3.25. Pp. 125, with 46 illustrations and 10 tables. Published by Child Development Publications of the Society for Research in Child Development, Inc., Purdue University, Lafayette, Indiana, 1961.

TRAITÉ DE TECHNIQUE CHIRURGICALE. Vol. III. By B. Fey, P. Mocquot, S. Oberlin, J. Quénu, P. Truffert, M. David, M. Iselin, R. Dossot, R. Dubar, Ch. Dubost, J.-J. Galey, Y. Longuet, J. Longue, J. Mathey, F. Palmer, J. Perrotin, J. Rudler, G. Thomeret, and J. Varangot. Cloth. Pp. 698, with 532 illustrations. Masson et Cie, Éditeurs 120 Boulevard Saint-Germain, Paris (6e), France, 1961.

ACTA ORTHOPAEDICA SCANDINAVICA, SUPPLEMENTUM No. 49. COMPARATIVE VALUE OF ELECTROMYOGRAPHIC, MYELOGRAPHIC AND CLINICAL-NEUROLOGICAL EXAMINATIONS IN DIAGNOSIS OF LUMBAR ROOT COMPRESSION SYNDROME. By Bertil Knutsson. Paper. Pp. 135, with 30 tables. Ejnar Munksgaard, Copenhagen, 1961.

ACTA ORTHOPAEDICA SCANDINAVICA, SUPPLEMENTUM No. 52. NERVOUS AND VASCULAR INFLUENCE ON LONGITUDINAL GROWTH OF BONE; AN EXPERIMENTAL STUDY ON RABBITS. By Henry Troupp. Paper. Pp. 78, with 42 illustrations. Ejnar Munksgaard, Copenhagen, 1961.

PROCEEDINGS OF THE FOURTH NATIONAL CANCER CONFERENCE. Sponsored by American Cancer Society, Inc. and National Cancer Institute, U. S. Public Health Service. Cloth. Price, $9.00. Pp. 774, with numerous illustrations. J. B. Lippincott Company, 227–231 S. Sixth Street, Philadelphia, Pa., 1961.

ACTA ORTHOPAEDICA SCANDINAVICA, SUPPLEMENTUM No. 44A. COMPARISON BETWEEN BIOLOGICAL ASSAYS AND THE FERROXYL TEST FOR STUDYING CORROSION OF EXPERIMENTAL METAL IMPLANTS. By Hans Emnéus. Paper. Pp. 15, with 5 figures and 2 tables. Ejnar Munksgaard, Copenhagen, Denmark, 1960.

THE SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION. VOL. 12—SUPPLEMENTUM 50. RATIONAL USE OF ANTIBIOTICS IN HOSPITALS; STUDIES ON LABORATORY METHODS AND DISCUSSION OF THE BIOLOGICAL BASIS FOR THEIR CLINICAL APPLICATION. By Hans Ericsson. Paper Pp. 59. Stockholm, Sweden, 1960.

THE SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION. VOL. 12—SUPPLEMENTUM 51. THE ADHESIVENESS OF HUMAN BLOOD PLATELETS IN VITRO. By Arvid John Hellem. Paper. Pp. 117. Islo, 1960.

THE SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION. VOL. 12—SUPPLEMENTUM 52. POLYUNSATURATED FATTY ACIDS IN MAN; SERUM, CUTANEOUS AND SUBCUTANEOUS LEVELS IN INDIVIDUALS WITH NORMAL AND ELEVATED SERUM LIPIDS. By Per Björntorp. Paper. Pp. 147. Oslo, 1960.

THE SCANDINAVIAN JOURNAL & LABORATORY INVESTIGATION. VOL. 12—SUPPLEMENTUM 53. THE EFFECT OF EDTA ON HUMAN FIBRINOGEN AND ITS SIGNIFICANCE FOR THE COAGULATION OF FIBRINOGEN WITH THROMBIN. By Hans Christian Godal. Paper. Pp. 20. Oslo, 1960.

THE SCANDINAVIAN JOURNAL OF CLINICAL & LABORATORY INVESTIGATION. VOL. 12—SUPPLEMENTUM 54. THE ELIMINATION OF URIC ACID IN MAN; STUDIED BY MEANS OF C^{14}-LABELED URIC ACID; URICOLYSIS, By Leif Bøge Sørensen. Paper. Pp. 214. Oslo, 1960.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: Deauville Hotel, Miami Beach, Fla., Sept. 26–29, 1961.

American Radium Society
Secretary, Dr. Charles G. Stetson, 350 Engle Street, Englewood, N. J. Annual meeting: Waldorf-Astoria Hotel, New York, N. Y., April 1–4, 1962.

Radiological Society of North America
Secretary, Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb.
Treasurer, Dwight Vincent Needham, 713 E. Genessee St., Syracuse, N. Y. Annual Meeting: Palmer House, Chicago, Ill., Nov. 26–Dec. 1, 1961.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois. Annual meeting: Roosevelt Hotel, New York, N. Y. Feb. 7–10, 1962.

Section on Radiology, American Medical Association
Secretary, Dr. Clyde A. Stevenson, Sacred Heart Hospital, West 101 Eighth Ave., Spokane 4, Wash. Annual meeting: Chicago, Ill., June 11–15, 1962.

American Board of Radiology
Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building, Rochester, Minn. The Fall 1961 examination will be held at the Shoreham Hotel, Washington, D. C., December 4–7, inclusive; the deadline for filing applications was July 1, 1961. A Special Examination in Nuclear Medicine will be offered if there are sufficient applications.

American Association of Physicists in Medicine
Secretary-Treasurer, Charles S. Simons, University of Michigan Hospital, Ann Arbor, Mich. Annual meeting to be announced.

Tenth International Congress of Radiology
Secretary-General, Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal 2, Quebec, Canada. Meets in Montreal, Aug. 26–Sept. 1, 1962.

Eighth Inter-American Congress of Radiology
Counselor for the United States, Dr. J. A. del Regato, Penrose Cancer Hospital, 2200 North Cascade Avenue, Colorado Springs, Colorado. Meeting to be announced.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

American Nuclear Society
Executive-Secretary, Octave J. Du Temple, 86 E. Randolph St., Chicago, Ill.

Arizona Radiological Society
Secretary, Dr. Don E. Matthieson, 926 East McDowell Rd., Phoenix, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists
Secretary, Dr. Herbert M. Stauffer, Temple University Medical Center, Philadelphia 40, Pa. Annual Meeting: University of Indiana, Indianapolis, Ind., May 19–20, 1962.

Atlanta Radiological Society
Secretary, Dr. Wilson T. Edenfield, 35 Linden Ave., N.E., Atlanta 8, Ga. Meets monthly, except during three summer months, on second Friday evening.

Blockly Radiological Society
Secretary, Dr. Samuel Finkelman, 101 S. Twentieth St., Philadelphia, Pa.

Brooklyn Radiological Society
Secretary, Dr. Joseph Arcomano, 168 Clinton St., Brooklyn 1, N. Y. Meets first Thursday of each month October through May.

Buffalo Radiological Society
Secretary, Dr. R. Joseph Naples, 106 Morgan Parkway, Williamsville 21, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Radiological Society
Secretary, Dr. Joseph A. Head, 150 Marshall St., Syracuse, N. Y. Meets first Monday each month October through May.

Central Ohio Radiological Society
Secretary, Dr. Robert L. Freidman, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, November, January, March and May at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine
Secretary, Dr. Robert S. Landauer, Radiation Center Building, 1903 West Harrison St., Chicago 12, Ill.

Chicago Roentgen Society
Secretary, Dr. William F. Hutson, 5145 N. California Ave., Chicago, Ill. Meets second Thursday of each month, October to April except December at the Sheraton Hotel at 8:00 P.M.

Cleveland Radiological Society
Secretary, Dr. Norman E. Berman, 14404 S. Park Blvd., Shaker Hgts. 20, Ohio. Meetings at 7:00 P.M. on fourth Monday of each month from October to April at Tudor Arms Hotel.

Colorado Radiological Society
Secretary, Dr. Seward Imes, 1845 High St., Denver, Colo. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. James L. Krieger, 85 Jefferson St., Hartford, Conn. Meets first Friday in February and April.

Dallas-Fort Worth Radiological Society
Secretary, Dr. F. J. Bonte, 5201 Harry Hines Blvd., Dallas 35, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit 1, Mich. Meets monthly first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

East Tennessee Radiological Society
Secretary, Dr. J. Marsh Frere, Jr., 205 Medica Arts Building, Knoxville, Tenn. Meets in January and September.

Eastern Conference of Radiology
Secretary, Arrangements Committee, Dr. Philip Myers, Baltimore City Hospital, Baltimore 24, Md. Annual meeting to be announced.

Eastern Radiological Society
Secretary, Dr. James F. Martin, North Carolina Baptist Hospital, Winston-Salem, N. C. Meets at Mid Pines Club, Southern Pines, N. C., April 29–May 2, 1962.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Florida Radiological Society
Secretary, Dr. Richard D. Shapiro, 1680 Meridian Ave., Miami Beach, Fla. Meets twice annually, in the spring with the annual State Society Meeting, and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Joseph C. Rush, 1800 Druid Rd., Clearwater, Fla.

Georgia Radiological Society
Secretary, Dr. George W. Brown, Griffin, Ga. Meets in spring and fall with Annual State Society Meeting.

Greater Miami Radiological Society
Secretary, Dr. Carl E. Balli, 907-8 Huntington Medical Building, Miami 32, Fla. Meets monthly third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary, Dr. William E. Powers, St. Louis, Mo.

Houston Radiological Society
Secretary, Dr. John Douglas Reeve, Texas Medical Center Library, Jesse H. Jones Library Bldg., Houston 25, Texas. Meets last Monday each month, Seminar Room, Doctors' Club of Houston.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the Spring and Fall.

Illinois Radiological Society
Secretary, Dr. George A. Miller, Carle Hospital Clinic, Urbana, Ill. Meets in spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. David E. Wheeler, 1500 North Ritter, Indianapolis, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. L. L. Maher, 1419 Woodland Ave., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. Roger K. Wallace, Riley County Hospital, Manhattan, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. Lawrence A. Davis, 226 East Chestnut St., Louisville, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Abraham Berens, 1917 Bedford Ave., Brooklyn 25, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Saul Heiser, Los Angeles, Calif. Meets second Wednesday of month in September, November, January, March and June at Los Angeles County Medical Association Building, Los Angeles.

Maine Radiological Society
Secretary, Dr. Albert A. Poulin, Thayer Hospital, Waterville, Maine. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Nathan B. Hyman, 1805 Eutaw Place, Baltimore 17, Md.

Memphis Roentgen Society
Secretary, Dr. Irving K. Ettman, Kennedy V.A. Hospital, Department of Radiology, Memphis 15, Tenn. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. William D. Roberts, 2197 Los Arrow Dr., Dayton 4, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
Secretary, Dr. Joseph Sorrentino, St. Francis Hospital, Poughkeepsie, N. Y. Meets 8:30 P.M., fourth Wednesday each month, September to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. Abraham Marck, Mayfair Professional Bldg., Milwaukee 13, Wis. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary, Dr. Donald H. Peterson, 855 Medical Arts Bldg., Minneapolis 2, Minn. Meets three times annually, in fall, winter and spring.

Mississippi Radiological Society
Secretary, Dr. Jack K. Goodrich, University Medical Center, Jackson, Miss. Meets third Thursday of each month at Hotel Edwards, Jackson, at 6:00 P.M.

Montana Radiological Society
Secretary, Dr. J. K. Boughn, 35 11th Ave., Helena, Montana. Meets at least once a year.

Nassau Radiological Society
Secretary, Dr. Robert Tugendhaft, 100 Nowbridge Rd., Hicksville, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska Radiological Society
Secretary, Dr. Ronald E. Waggener, The Radiologic Center, Nebraska Methodist Hospital, Omaha 31, Nebraska. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Robert E. Wise, 605 Commonwealth Ave., Boston 15, Mass. Meets third Friday of each month, October through April at The Longwood Towers, Brookline, Mass.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly

New York Roentgen Society
Secretary, Dr. Bernard Wolf, Mt. Sinai Hospital, New York, N. Y. Meets monthly on third Monday, New York Academy of Medicine at 4:30 P.M.

North Carolina Radiological Society
Secretary, Dr. A. B. Croom, 624 Quaker Lane, High Point, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. R. F. Raasch, Post Office Box 990, Dickinson, North Dakota. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Lester I. Citrin, St. Mary's Hospital, Troy, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

Northern California Radiological Society
Secretary, Dr. Rob H. Kirkpatrick, 1219 28th St., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Northwestern Ohio Radiological Society
Secretary, Dr. George Asahina, 421 Michigan St., Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Paul D. Meyer, 125 S. Grant Ave., Columbus, Ohio. Annual meeting to be announced.

Oklahoma State Radiological Society
Secretary, Dr. Simon Pollack, Utica Square Medical Center, Tulsa, Okla. Meets in January, May and October

Oregon Radiological Society
Secretary, Dr. George R. Satterwhite, Willamette Falls Community Hospital, 15th and Division, Oregon City, Ore. Meets monthly from October to June on the sec-

ond Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. John N. Burkey, 555 Dental Bldg., Seattle, Wash. Annual meeting: Seattle, Washington.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco 8, Calif. Meets annually during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. Frederick R. Gilmore, Clearfield Hospital, Clearfield, Pa. Annual meeting: Pocono Manor Inn, May 25–26, 1962.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Robert B. Funch, Department of Radiology, Germantown Hospital, Philadelphia 44, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Ross H. Smith, St. Margaret Memorial Hospital, Forty-Sixth St., Pittsburgh 1, Pa. Meets second Wednesday of month, October through June at Park Schenely Restaurant.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. James K. V. Willson, 1100 N. Charles St., Baltimore 1, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Donald Janny, Cincinnati, Ohio. Meets monthly from September to May on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. G. J. Liese, Queen's Hospital, Honolulu, Hawaii. Meets third Monday of each month at 7:30 P.M.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. Robyn Hardy, 4324 Magnolia St., New Orleans 15, La. Meets annually during Louisiana State Medical Society meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. George H. Burke, 601 Grand Ave., Asbury Park, N. J. Meets at Atlantic City at time of State Medical Society meeting and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester 18, N. Y. Annual meeting to be announced.

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. Joseph F. Linsman, 436 N. Roxbury Dr., Beverly Hills, Calif.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY
Secretary, Dr. Lee E. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Robert H. Greenlaw, 260 Crittenden Blvd., Rochester 20, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Freed, 4200 East Ninth Ave., Denver 20, Colo. Annual meeting to be announced.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets third Wednesday each month in Fort Sam Houston Officer's Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY
Secretary, Dr. Stanley A. Moore, 2466 First Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. M. A. Sisson, 450 Sutter St., San Francisco 8, Calif. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco 18, Calif.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

SECTION ON RADIOLOGY, CONNECTICUT STATE MEDICAL SOCIETY
Secretary, Dr. Wayne P. Whitcomb, Hospital of St. Raphael, New Haven, Conn. Meetings are held bimonthly.

SECTION ON RADIOLOGY, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. William E. Sheely, 1746 K St., N.W., Washington 6, D. C. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. William Meszaros, 1825 W. Harrison St., Chicago, Ill.

SECTION ON RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Seymour Ochsner, Ochsner Clinic, 3503 Prytania St., New Orleans 15, La. Annual meeting to be announced.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY
Secretary, Dr. Richard G. Lester, 412 Union St., S.E., Minneapolis 14, Minn. Annual meeting: Deauville Hotel, Miami Beach, Fla., Sept. 25, 1961.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Dr. Robert W. Lackey, 452 Metropolitan Bldg., Denver 2, Colo. *Administrator*, Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting: Baker Hotel, Dallas, Texas, June 27–30, 1962.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. Stanford B. Rossiter, 1111 University Dr., Menlo Park, Calif. Meets second Wednesday of each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTHERN RADIOLOGICAL CONFERENCE
Secretary, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala.

SOUTHWESTERN RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph S. Clayton, 1501 Arizona, Bldg. 2-A, El Paso, Texas. Meets second Tuesday of each month.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. B. M. Brady, St. Joseph Hospital, Memphis, Tenn. Meets annually at the time and place of the Tennessee State Medical Association meeting.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 402 Professional Bldg., 1216 Pennsylvania Ave., Fort Worth 4, Texas. Annual meeting: Austin, Texas, Jan. 19 and 20, 1962.

Tri-State Radiological Society
Secretary, Dr. John Marchand, 118 S.E. First St., Evansville, Ind. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary, Dr. Richard Y. Card, St. Mark's Hospital, Salt Lake City, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. Powell G. Dillard, Jr., 715 Church Street, Lynchburg, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Joseph T. Houk, 14303 Ambaum Blvd., Seattle 66, Wash. Meets third Monday of each month from September through April at the University of Washington Medical School.

West Virginia Radiological Society
Secretary, Dr. Karl J. Myers, 112 N. Woods St., Philippi, W. Va. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. Anthony A. Maglione, Westchester Academy of Medicine, Section on Radiology, Purchase, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. Howard G. Bayley, 116 Iroquois Parkway, Beaver Dam, Wis. Annual meeting each spring in various places.

Cuba, Mexico, Puerto Rico and Central America

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Julio Toriello, 11 Calle 2-37, zona 1, Guatemala. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Rafael Vega Gómez.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad de Radiología y Fisioterapía Cubana
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

Sociedad Costarricense de Radiologia
Secretary, Dr. James Fernández Carballo, Apartado VIII, San José, Costa Rica.

Sociedad Mexicana de Radiología, A. C.
Calle del Oro No. 15, México 7, D. F
Secretary-General, Dr. E. Alvarez Hernández. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. César E. Rosa-Perez, Fondo del Segura del Estado, Parada 1, San Juan 8, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. Odilon Raymond, 5400 Blvd. Gouin. Quest, Montreal, Que. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. R. D. Hoare, 32 Welbeck St., London, W. 1. Meets monthly from October until May.

Edmonton and District Radiological Society
Secretary, Dr. S. C. Windle, 105 Northgate Bldg., Edmonton, Alberta. Meets first Tuesday of each month, Oct. to May.

Faculty of Radiologists
Honorary Secretary, Dr. R. A. Kemp Harper, 47 Lincoln's Inn Fields, London, W.C.2, England. Annual meeting to be announced.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Canadian Association of Radiologists
Honorary Secretary, Dr. Robert G. Fraser. *Associate Honorary Secretary*, Dr. Jean-Louis Léger, 1555 Summerhill Ave., Montreal 25, Que. Annual meeting: Marlborough Hotel, Winnipeg, Man., Jan. 22–24, 1962.

Montreal Radiological Study Club
Secretary, Dr. F. McConnell, 1650 Cedar Ave., Montreal, Quebec. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicale
General Secretary, Dr. Maurice Dufresne, 1560 Sherbrooke (East), Montreal, Canada. Meets third Saturday each month.

Toronto Radiological Society
Secretary, Dr. Wallace M. Roy, St. Joseph's Hospital, 30 The Queensway, Toronto 3, Ontario. Meets second Monday of each month September through May.

College of Radiologists of Australia
Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Institute de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional del Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, D. Camillo Segreto. Avenida Angélica, 1.170, Caixa Postal 5984, São, Paulo, Brazil.

Sociedad Argentina de Radiología, Junta Central, Buenos Aires
Secretary, Dr. Edgardo O. Olcese, Santa Fé 1171, Buenos Aires. Meetings are held monthly.

Sociedad Bolivana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1596, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl. Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. J. P. Velasco, Avenida Santa María 0410, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Mejía Diazgranados, Carrera 13, No. 25–31, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Publio Vargas P., Casilla 1242, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary, Dr. Luis Pinillos Ganoza, Apartado 2306, Lima, Perú. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

Sociedad de Radiologia del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiologia.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Ernesto H. Cibils, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiologia de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenologia y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Carlos A. Oulton, Santa Rosa 447, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Rubén Merenfeld, Apartado No. 9362, Candelaria, Caracas, Venezuela. Meets monthly third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 256 Chaussée de Wavre, Heverlee-lez-Louvain, Belgium. Meets in February, March, May, June, October, November and December.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris.
Secretary-General, Dr. Ch. Proux, 9, rue Daru, Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Šrobárova 50, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgengesellschaft
Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut. Lagenbeckstr. 1, Mainz, Germany. Annual meeting to be announced.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Electrologie en Röntgenologie
Secretary, Dr. J. R. von Ronnen, Violenweg 14, den Haag, Netherlands.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Española de Radiología y Electrología Médicas y Medicina Nuclear
Secretary, Dr. D. Aureo Gutierrez Churruca, Esparteros, No. 9, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Cecchini, A., and De Donato, E. I meningiomi delle docce olfattorie. (Meningiomas of the olfactory grooves.) *Radiol. med.*, Dec., 1960, *46*, 1150–1158. (From: Reparto Radiologico, Istituto Neurologico "Carlo Besta" di Milano, Italy.)

The authors present an analysis of the roentgenologic findings in meningiomas of the olfactory grooves, as noted on routine roentgenograms of the skull, or on roentgen studies of the central nervous system with contrast media. Nine cases were males and 17 females; the average age at the time of admission was forty-six years. Surgical intervention showed that in 7 cases the meningioma involved only one olfactory groove, while in 10 cases the involvement was bilateral, and in 9 cases, although the meningioma involved both olfactory grooves, there was a greater involvement on one side.

The roentgen findings noted on plain skull roentgenograms are several: (1) calcifications were present in 5 cases (19.2 per cent), and all appeared above the ethmoidal-sphenoidal plane; (2) localized condensation of bone was present in 15 cases (57.6 per cent)—from a simple osteosclerosis (7 cases, 26.9 per cent), to a thickening of the floor of the anterior fossa (6 cases, 23 per cent), or to a localized hyperostosis (2 cases, 7.7 per cent). These changes were in 11 cases limited to the midline and were symmetric, in the remaining 4 cases they involved only one side; (3) localized osteolytic lesions were noted only in 2 cases, in both at the point of origin of the meningioma; and (4) bony lesions secondary to increased intracranial pressure were present in 18 cases (69.2 per cent).

The roentgen findings in cerebral angiography are such as to permit a correct diagnosis of the site and nature of a meningioma of the olfactory groove. The most common sign is a posterior displacement of the anterior cerebral artery and its frontal branches, as it appears on the lateral angiograms. The angiographic findings in the anteroposterior view depend on the site and extent of the meningioma. In the venous stage there is a posterior displacement of the central veins. In only 8 cases (30.7 per cent) was there pooling of the contrast medium in correspondence with the site of the meningioma. In 12 cases (46.1 per cent) there was involvement of the ophthalmic artery and its branches.

Pneumoencephalography was performed in only 10 cases and generally at the beginning of the clinical investigation and before cerebral angiography. The characteristic findings are an indentation produced by the neoplasm on the frontal horn or horns and on the anterior part of the third ventricle; these were present in 8 cases. The cisterns in the region of the sella turcica were involved in 7 cases; in a few patients there was a block at the level of the cisterna chiasmatis and of the lamina terminalis, which, however, were always displaced posteriorly. In 1 case there was a complete cisterno-ventricular block.

In the opinion of the authors, the roentgen findings observed on plain skull roentgenograms and on cerebral angiograms are in almost all cases sufficient to make the correct diagnosis. In certain cases, in the so-called olfactory-tubercular meningiomas, the neoplasm cannot easily be differentiated from a meningioma arising from the tuberculum sellae. The glioma of the chiasm, the craniopharyngioma, the chordoma of the clivus, etc. have characteristics which differentiate them from the meningioma of the olfactory grooves.—*A. F. Govoni, M.D.*

Keirns, M. M. The angiographic demonstration of cerebral occlusive disease. *South. M. J.*, May, 1961, *54*, 470–475. (From: The Department of Radiology, Baptist Memorial Hospital, Memphis, Tenn.)

The author and his associates have performed 3,000 angiographic studies of the intracranial and neck vessels. Of these cases, only 0.8 per cent died or had permanent hemiplegia within twenty-four hours after the angiographic procedure; several of them had pre-existing disease sufficient to cause death. An additional 2 per cent had mild reactions with complete recovery.

The six methods used were: (1) direct percutaneous injection of the common carotid and the vertebral arteries; (2) retrograde carotid injection accomplished by compressing the carotid artery distal to the needle, thereby demonstrating its origin; (3) vertebral injection; (4) direct subclavian injection; (5) retrograde catheterization of the innominate artery through the right carotid; and (6) brachial artery catheterization. The brachial and direct subclavian injections are not considered to be satisfactory methods. Pneumothorax and mediastinal hemorrhage occurred too often with subclavian punctures. Over 40 per cent of the patients experienced mediastinal hemorrhage.

Three types of occlusive disease occur in the neck and head vessels: (1) localized plaque formation, (2) multiple widespread plaque formation, and (3) generalized constriction of many cerebral vessels. The association of some of these lesions with various types of strokes is discussed.—*Frank M. Windrow, M.D.*

Crawford, E. Stanley, DeBakey, Michael E., Morris, George C., Jr., and Fields, William S. Treatment of stroke by arterial reconstructive operation. *South. M. J.*, May, 1961, *54*, 476–485. (From: The Cora and Webb Mading Department of Surgery and the Department of Neurology, Baylor

University College of Medicine, Houston, Tex.)

Angiographic studies were done on 895 patients in whom extracranial lesions were suspected. Lesions were demonstrated in 336 of these cases. Bilateral carotid and bilateral trans-subclavian vertebral angiography was done on 861 consecutive patients. Thoracic angioaortography was performed when occlusion at the origin of the vessels from the aorta was suspected. The common sites of occlusion were at the bifurcation of the common carotid, at the origin of the common carotid, or at the origin of the vertebral, innominate or subclavian arteries.

Seventeen patients were treated because of troublesome ear noises or systolic murmurs in the neck. There were 292 patients with neurologic disturbances. The neurologic findings are quite variable due to multiple occlusive changes and also to the variable collateral circulation. The classic symptoms produced by occlusion of the various vessels are outlined by the authors. Systolic murmurs are frequently heard at the site of partial occlusions. Diminished pulsation of the vessels and diminished blood pressure distal to involved vessels are important physical findings. The authors suggest routine angiographic studies of all patients who have suffered a stroke.

Of the 458 lesions treated surgically, 12 involved the external carotid, 309 the internal carotid, 20 the common carotid, 23 the innominate, 41 the subclavian and 53 the vertebral arteries. Operability depended on the location and extent of the occlusion and the status of the peripheral vessels. Patients with transient ischemic attack, strokes which have cleared and strokes with progressive improvement have a good prognosis. Others usually have multiple lesions and respond less satisfactorily to reconstructive vascular surgery.

The two procedures usually employed were endarterectomy and end-to-side bypass graft. The techniques of each procedure, the anesthesia and the postoperative care are discussed.

The surgical results are tabulated and discussed. They show a remarkable improvement in the prognosis for patients afflicted with strokes.—*Frank M. Windrow, M.D.*

Keirns, M. M. Radiologic diagnosis of intracranial aneurysms and vascular malformations. *South. M. J.*, May, 1961, *54*, 485–492. (From: The Department of Radiology, Baptist Memorial Hospital, Memphis, Tenn.)

In the past twelve years 3,000 cerebral arteriographies were done; 140 aneurysms and 22 arteriovenous malformations were diagnosed.

Aneurysms are visualized as small pools of contrast material lying outside the usual contour of the normal vessel, most commonly in the vicinity of a bifurcation and frequently in the circle of Willis. Bleeding is evidenced by displacement of vessels or a small "teat-like" protrusion of the opaque medium from the aneurysm. Spasm of a vessel is indirect evidence of bleeding. Because of the frequency of multiple lesions it is necessary to determine the exact point of origin of the bleeding if possible. Oblique roentgenograms sometimes help to demonstrate the neck of the aneurysm. "Berry aneurysms" found about the circle of Willis are due to congenital malformations and are found in young people. Arteriosclerotic aneurysms are usually along the course of a vessel in patients over thirty years of age.

It is desirable to determine whether cross-filling of the aneurysm occurs from the opposite side in order to properly treat the case. Both the carotid and vertebral arteries should be demonstrated because of the frequency of multiple aneurysms.

Arteriovenous malformations show large dilated feeding arteries, serpiginous vessels in the lesion, and very rapid transit of contrast material through the lesion.

The definitive diagnosis of intracranial aneurysms or arteriovenous malformations is almost wholly dependent on cerebral arteriography.—*Frank M. Windrow, M.D.*

Neck and Chest

Arcilla, Rene A., and Gasul, Benjamin M. Congenital aplasia or marked hypoplasia of the myocardium of the right ventricle (Uhl's anomaly); clinical, angiocardiographic, and hemodynamic findings. *J. Pediat.*, Mar., 1961, *58*, 381–388. (From: The Pediatric Cardiophysiology Department, Cook County Children's Hospital and Hektoen Institute for Medical Research, and the Department of Pediatrics, University of Illinois College of Medicine, Chicago, Ill.)

The authors report the angiocardiographic and hemodynamic findings in a proved case of congenital aplasia or marked hypoplasia of the myocardium of the right ventricle.

The clinical findings consisted of progressive heart failure in infancy, marked cardiomegaly, feeble triple heart tones, no significant murmur, and absence of clinical evidence of right ventricular hypertrophy, pulmonary hypertension, or tricuspid regurgitation. The chest roentgenograms demonstrated marked cardiac enlargement with normal or diminished pulmonary vascular markings. The electrocardiogram showed right atrial hypertrophy and left ventricular hypertrophy. Cardiac catheterization revealed normal systolic pressures and markedly elevated presystolic waves in the right ventricular and pulmonary arterial pressure curves which were identical with the right atrial "a" waves.

The angiocardiograms demonstrated enlarged right heart chambers, diminished pulmonary blood

flow, unusual thinness of the right ventricular wall, and conspicuous absence of its trabeculae.

The authors suggest a superior vena cava-right pulmonary artery anastomosis for palliative treatment of this anomaly.—*James F. Martin, M.D.*

Löhr, H., Loogen, F., and Vieten, H. Die periphere Pulmonalstenose. (Peripheral pulmonary stenosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Mar., 1961, *94*, 285–304. (Address: Prof. Dr. H. Vieten, Moorenstr. 5, Düsseldorf, Germany.)

Peripheral pulmonary stenosis, as defined by the authors of this article, refers to any stenotic area distal to the pulmonary valve in the course of the pulmonary arterial circulation. It includes single or multiple lesions. The recorded incidence of this condition is relatively small, chiefly because of the paucity of symptoms and because associated cardiovascular anomalies frequently dominate the clinical picture and diagnostic methods.

Three main types are recognized: Form I includes single or multiple stenoses of the pulmonary artery of lobar, segmental, or lesser caliber; Form II refers to stenoses of one or both main pulmonary arteries at varying distances from the main stem and usually associated with marked post-stenotic dilatation of the involved vessel; Form III comprises stenoses of the supravalvular portion of the main stem that are not accompanied by any appreciable post-stenotic dilatation.

Of 1,500 patients with congenital vascular anomalies, peripheral pulmonary stenosis was found in 0.44 per cent. In this study, only those cases with isolated peripheral pulmonary stenosis were considered with regard to the hemodynamics, clinical picture, prognosis and differential diagnosis.

The hemodynamics in stenosis of a single peripheral artery is essentially normal, whereas in Form III it is similar to pulmonary valvular stenosis. The findings in Form II are not remarkable under normal conditions with the patient at rest. Occasionally, in Form II there may be a pressure difference in the systolic phase between pre- and post-stenotic levels, but the measurements are equal during diastole.

The most reliable diagnostic method is selective intravascular catheterization. With this procedure, if there is a diastolic as well as a systolic differential in a main pulmonary branch, one should suspect stenosis of the contralateral main branch or multiple stenoses in the contralateral lung. If both main stems are stenotic, it is rare to find any marked prestenotic hypertension. This is also true for supravalvular stenosis.

The clinical picture depends on the height of the pressure. If the pressure is low, symptoms are usually absent. Patients with high grade hypertension have exertional dyspnea, marked cyanosis and easy fatigability. Intravascular phonocardiography is particularly valuable in ascertaining the type of murmur. A pure systolic murmur is a frequent finding. A continuous systolic and diastolic murmur is typical and is always registered in the post-stenotic portion. The roentgen findings include a prominent pulmonary artery segment and wide central and fine peripheral vessels in the lungs, with or without dilatation of the right side of the heart.

While supravalvular stenosis is quite similar to pulmonary valvular stenosis, the latter is not associated with a prominent pulmonary artery segment but does produce a loud P_2 sound, which is of diagnostic help. Because of the type of murmur, peripheral pulmonary stenosis must be distinguished from patent ductus, particularly if the murmur is maximal in the second left intercostal space in the parasternal line. Patent ductus is associated with increased pulmonary vascularity. Such entities as arteriovenous fistula, aortopulmonary septal defect and pulmonary thrombosis are most easily differentiated by means of angiocardiography and selective catheterization.—*J. Zausner, M.D.*

Johnson, Philip M., Wood, Ernest H., Pasternack, Bernard S., and Jones, Morris A. Roentgen evaluation of pulmonary arterial pressure in mitral stenosis. *Radiology*, Apr., 1961, *76*, 541–547. (Address: P. M. Johnson, 141 Central Avenue, Montclair, N. J.)

The purpose of this paper is to review attempts made in the past to relate roentgen findings to pulmonary arterial pressure and to report the value of newly devised multiparameter formulas for the purpose.

Roentgenograms of the chest give reliable quantitative evidence of pulmonary hypertension in mitral stenosis. As pointed out by Kerley, the peripheral basal linear markings, which he called B-lines, may be produced by pulmonary venous hypertension. The development of B-lines in mitral stenosis is presumptive evidence of pulmonary venous hypertension. Their occasional presence during left ventricular failure and chronic passive congestion has been noted. B-lines are usually seen in cases with pulmonary "capillary" pressures above 20 to 30 mm. Hg and are invariably present when the mean left atrial pressure is in excess of 24 mm. Various investigators have measured the width of the upper portion of the descending branch of the right pulmonary artery to determine the relationship between pulmonary arterial pressure and vessel width. It was concluded that the upper limit of normal width was 14 mm. Significant pulmonary hypertension was found in all patients with a vessel width of 15 mm. or more.

Forty-eight patients with pure or predominant mitral stenosis, as established by clinical, laboratory, and cardiac catheterization findings, were investi-

gated by the authors. Measurements of resting mean pulmonary arterial and pulmonary "capillary" pressures were made on all patients. In each patient an erect 2 m. posteroanterior chest roentgenogram, made within a few days after cardiac catheterization, was available for study. From this the following data were obtained: the presence or absence of B-lines; the altitude in millimeters of the pulmonary artery segment; the width in millimeters of the right descending pulmonary artery branch; the "pulmonary arterial size" in centimeters; and the internal thoracic diameter. Regression equations were derived which gave a strong correlation between mean resting pulmonary arterial pressure and four roentgen parameters: the presence or absence of Kerley's B-lines, the height in millimeters of the pulmonary artery segment, the width in millimeters of the right descending pulmonary artery segment branch, and the "pulmonary arterial size" in centimeters.—*A. W. Sommer, M.D.*

McCue, Carolyn M., and Young, R. B. Cardiac failure in infancy. *J. Pediat.*, Mar., 1961, *58*, 330–341. (From: The Department of Pediatrics, Medical College of Virginia, Richmond, Va.)

The authors present a review of 115 consecutive cases of cardiac failure in infancy to emphasize the serious prognosis of congestive heart failure and to stress the importance of early definitive diagnosis.

The primary causes of congestive cardiac failure in 71 per cent of the cases studied were endomyocardial disease, interventricular septal defect, coarctation of the aorta, transposition of the great vessels, patent ductus arteriosus, and aortic atresia. The term "cardiac failure" was used to indicate that the heart had failed to maintain adequate output to supply the metabolic needs of the body. Dyspnea was always present and a cardiac enlargement was noted in all but a few cases.

The following therapeutic principles and/or measures constituted the initial management: (1) oxygen, (2) rest, (3) antibiotics, (4) low salt diets, (5) diuretics, and (6) digitalis.

Although the prognosis for infants with cardiac failure is grave, it seems clear that a progressively larger percentage of them can be salvaged by identification of the underlying lesion and by adequate treatment. This is notably true in respect to patent ductus arteriosus, coarctation of the aorta, paroxysmal supraventricular tachycardia, pulmonic stenosis, myocarditis, and severe anemia.—*James F. Martin, M.D.*

Thurn, P., Schaede, A., Hilger, H. H., and Düx, A. Der Ventrikelseptumdefekt im selektiven Laevokardiogramm. (Ventricular septal defect in selective levocardiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Mar., 1961, *94*, 305–323. (Address: Prof. Dr. P. Thurn, Med. Klinik der Univ., Bonn-Venusberg, Germany.)

Selective levocardiography is the best method for accurate localization of ventricular septal defects with left to right shunt, whether isolated or multiple defects exist. It is particularly valuable when the defect is small, since this method can distinguish membranous from muscular defects. It is likewise definitive for the differential diagnosis of isolated intra-atrial septal defect and one combined with a ventricular septal defect. Also, a common atrioventricular channel can be differentiated from a combined intra-atrial and ventricular septal defect, particularly with the direct opacification of the right atrium from the left ventricle. In addition, levocardiography is successful in demonstrating aortic valvular insufficiency with subvalvular septal defect and differentiating this combination from ductus arteriosus or aortopulmonary defects.

Selective levocardiography affords the advantage of an unobstructed view of the outflow tract of the right and left ventricles. There are no overlying pulmonary vessels. Opacification is maximal because there is no dilution of the contrast material in the lungs or the left atrium. A rapid filming technique is essential. The best topographic results are obtained by simultaneous exposures in lateral and left anterior views. These projections also furnish information concerning the size of the defect, the caliber of the aorta and the ratio of the aortic to pulmonary diameter. In general, the size of the defect is less important than its proportional relationship to the diameter of the aorta.

In membranous defects, the contrast material flows from the left into the right ventricle chiefly in a caudal direction on the posterior wall, leaving the anterior wall (outflow tract) relatively unaffected. The shunted blood flows during systole in a dorsocaudal direction, whereas the diastolic flow occurs in the ventrally situated outflow tract. It has been determined that, in membranous defects, the shunt occurs during ventricular systole, while the shunt takes place during ventricular diastole if the defect is muscular and especially when it is small. Incidentally, a small muscular defect is of no real significance, since it usually closes during systole.

A dilated left ventricle associated with a relatively small aorta and wide pulmonary artery indicates a large left to right shunt, which will produce better contrast filling of the pulmonary arteries than a small left to right shunt. A slightly dilated left ventricle, with an aorta and pulmonary artery of equal caliber, indicates a weak shunt. A very marked dilatation of the left ventricle is usually combined with a ventricular and atrial septal defect.

A common atrioventricular chamber with an atrial septal defect produces a left to right shunt. The common chamber with a ventricular septal defect

will do likewise as long as the resistance in the lesser circulation is lower than in the general circulation. In this anomaly, during systole, the shunt is usually from the left ventricle to the right atrium, but, occasionally, it is from the right ventricle to the left atrium or from the left atrium to the right ventricle. An associated anomaly of the mitral valve may cause a shunt from the left ventricle to the left atrium. Similarly, an anomaly of the tricuspid valve may cause a reflux from the right ventricle to the right atrium. If an associated ventricular septal defect is not appreciable, the shunt is from the left ventricle to the right atrium. With a large ventricular septal defect, two shunts may be seen: from the left ventricle to the right atrium and simultaneous filling of the pulmonary artery and right atrium. This occurs particularly if there is a high septal defect.—*J. Zausner, M.D.*

Lehman, J. Stauffer. An evaluation of cardiovascular contrast media. *Radiology*, Apr., 1961, *76*, 548–563. (Address: 230 N. Broad Street, Philadelphia 2, Pa.)

The increased use of cardiovascular opacifying procedures for the diagnosis of congenital malformations of the heart and great vessels and for the study of acquired cardiovascular disease has led to a search for and development of many new radiopaque media. None of the methods of evaluating these conditions is completely devoid of danger to the patient and most of the hazards are due to the injected radiopaque medium. Because of this, the author has investigated the physicochemical and toxicologic properties of the various contrast media he has used in his clinical studies of the heart, intrathoracic vessels and pulmonary circulation. Since a good contrast agent should possess, in addition to an absence or low degree of toxicity, good radiodensity and low viscosity, and hence easy injectability, additional studies were made from the standpoint of viscosity, flow rates through catheters, phantom radiodensity and comparative angiocardiographic opacification in experimental animals. Reactions were also tabulated in a series of clinical studies made with certain of the media.

The viscosity studies were conducted at three different temperatures. They revealed that hypaque sodium 50 per cent had the lowest and cardiografin 90 per cent the highest viscosity. The viscosity of each of the media tested decreased as the temperature was raised. Flow rates through catheters were influenced most by the size of the catheter. Large bore catheters, at the high injection pressure applied, permitted a high rate of flow of each of the tested solutions, closely approximating that of water. As the catheter bore was decreased, differences in the rate of flow became more evident. Cardiografin 90 per cent was found to have the slowest rate of flow, while hypaque-M 50 per cent and miokon sodium 50 per cent were found to have the most rapid rates.

Animal toxicity studies showed that the cerebrotoxic and cardiotoxic effects are somewhat dependent upon the chemical nature and concentration of the contrast agent, more dependent upon the amount injected, and to a certain extent upon the site of injection. These studies were limited to toxicity comparisons of two of the newer preparations, ditriokon and renovist, with two of the older media, diodrast 70 per cent and urokon 70 per cent. Ditriokon and renovist were found to be less toxic to the animals (dogs) tested than diodrast 70 per cent.

Radiodensity studies were done with the use of a plastic block phantom as well as a testing procedure employing dogs under conditions simulating clinical cardiovascular opacification studies. While electronic densitometer recordings showed lower, medium and higher range radiopacity readings in the phantom procedure, the test procedure on dogs showed little over-all difference in the degree of opacification produced by the several media as determined visually.

Clinical studies for the most part with ditriokon, renovist, and hypaque 75 per cent have given the general impression that the incidence of reactions is about the same for all and that the degree of such reactions is very similar. The author believes that the reactions are definitely less marked as compared with his previous experiences using the more concentrated media such as diodrast 70 per cent and urokon 70 per cent. A considerably wider margin of safety is also felt to be present with the less concentrated media.

It is the opinion of the author that factors such as catheter type, size and length, pressure injection, injection rate, catheter positioning, rapid serial roentgenography or cineroentgenography, the amount of injected medium, and the technique of injection using the most favorable catheter location for the most informative study are of more importance and significance than minor differences in absolute radiodensity and small variations in iodine content of the several cardiovascular radiopaque agents. He concludes with the statement that renovist, of moderate iodine content, effective radiodensity, comparatively low viscosity, and a good flow rate through catheters appears to be one of the most satisfactory cardiovascular contrast preparations he has employed.—*Donald N. Dysart, M.D.*

Doyle, F. H., Read, A. E., and Evans, K. T. The mediastinum in portal hypertension. *Clin. Radiol.*, Apr., 1961, *12*, 114–129. (From: The Departments of Radiodiagnosis and Medicine, Hammersmith Hospital, London W.21, and Postgraduate Medical School of London, England.)

In portal hypertension due to intrahepatic or extrahepatic obstruction, some of the blood returning from the splanchnic bed bypasses the liver and is

shunted by collateral channels to the systemic venous system. These collateral channels ultimately drain into the superior and inferior venae cavae. The terminal part of the azygos vein, which joins the superior vena cava a short distance above the pericardium, is the "final common path" of all these routes. Any prolonged and considerable increase in the volume of blood flowing through the azygos and hemiazygos veins might be expected to result in an increase in their diameters.

The azygos vein in the thorax runs in a cephalad direction anterior to the vertebral bodies as far as the fourth or fifth dorsal vertebra. It is joined in front of the vertebral column by the superior and inferior hemiazygos veins. At the level of the fourth or fifth thoracic vertebral body, the azygos vein arches forward over the root of the right lung, passes close to the trachea in the right tracheobronchial angle, and joins the superior vena cava on its posterior aspect.

The method used in this study for the roentgen demonstration of the azygos vein was that of anteroposterior laminagraphy. The segment of the azygos vein which lies in the right tracheobronchial angle adjacent to the trachea is peculiarly well suited to laminagraphic demonstration. Its lateral margin is covered by mediastinal pleura and is clearly delineated against the aerated lung. The medial margin is not normally discernible, but the inner wall of the trachea is sharply defined against the shadow of air in the trachea. The size of the azygos vein shadow is largest when the patient is supine, smallest when the patient is erect, and intermediate when the patient is sitting. The exposure is made without delay at the end of a normal expiration—the size of the azygos vein being larger in expiration than in inspiration. Three laminagraphic sections are routinely made at intervals of 1 cm. using a multisection cassette. Nearly always the azygos vein is shown best in sections at levels 8, 9 or 10 cm. above the table top.

The criteria of portal hypertension accepted for this investigation were that the patient should have evidence of esophageal or gastric varices on barium swallow and/or collateral channels demonstrated by splenic venography. However, these criteria do not in every instance imply a raised portal pressure. In some cases of portal obstruction, the collateral vessels develop to such an extent that the portal pressure falls to normal levels.

The measured diameters of the azygos veins were plotted against age, sex, height, weight and body surface area and the only significant correlation was found to be with the weight of the patient. This correlation is statistically highly significant. Because of this finding, the diameters of the azygos veins in both control and portal hypertensive groups were corrected to a standard patient weight of 140 pounds. If all other causes of azygos vein enlargement are excluded, a patient with an azygos vein diameter of 20 mm. or more, measured by the method described, is almost certain to have portal hypertension.

The hemiazygos venous system is commonly represented as a superior and an inferior hemiazygos vein, each lying in front of the left side of the thoracic vertebral bodies and each draining into the azygos vein in front of the vertebral column. Explanations for the formation of the left paravertebral shadow seen on an anteroposterior roentgenogram of the thoracic spine vary. Billing and Knutsson imply that it is due to the pleural reflection between the descending aorta and the vertebral column. Gladnikoff, in his monograph on the mediastinum, introduces evidence to suggest that it is due to the hemiazygos vein. At all ages the left paravertebral shadow is, on the average, wider in the patient with portal hypertension than in the control group. Above the age of forty-five years, some factor or factors unrelated to portal hypertension are present which result in widening of the left paravertebral shadow. The factor which seemed to the authors to be the main cause for this was the presence of degenerative disk changes in the thoracic spine. Dilatation and elongation of the descending thoracic aorta is a second factor which may play a part in some cases. In reviewing the roentgenograms of a large series of patients with portal hypertension, a number of cases with very wide left paravertebral shadows were discovered. In all these patients there was clinical evidence of fluid retention, and it seemed plausible to the authors that the explanation of the abnormal width and shape of the left paravertebral shadow in this group lay in the presence of excess fluid in the mediastinum- "mediastinal edema."

The incidence of posterior mediastinal opacities or an abnormal right paravertebral shadow in patients with portal hypertension is not high—approximately 10 per cent. These mediastinal abnormalities occur (invariably, in the authors' experience) in patients who have large esophageal varices demonstrated by barium swallow, and who exhibit numerous large collateral venous channels at splenic venography. The lack of correlation between the size of the azygos vein and the extent of esophageal varices may be an indication that the flow of blood through the esophageal varices is slow, and that they are "poor collaterals," playing little part in reducing portal venous pressure. There is also an absence of correlation between the size of the azygos vein and the presence or absence of ascites, encephalopathy and gastrointestinal bleeding. Some estimate of the size of the azygos vein and of the width of the left paravertebral shadow can often be obtained from a supine anteroposterior roentgenogram of the mediastinum.

While roentgen study of the mediastinum can make an important contribution to the diagnosis of portal hypertension, these mediastinal abnormalities should not be misinterpreted. A dilated azygos vein in the tracheobronchial angle can simulate a tumor. Similarly, a dilated part in the ascending azygos vein

and in other mediastinal veins can simulate tumors. —*Samuel G. Henderson, M.D.*

Abdomen

Hays, Daniel M. Intussusception as a postoperative complication in pediatric surgery. *Surg., Gynec. & Obst.*, May, 1961, *112*, 583–589. (From: The Division of General Surgery, Los Angeles Childrens Hospital, Los Angeles, Calif.)

The author presents 9 cases in which the complication of intussusception occurred during the early postoperative state after laparotomy for other conditions. The cases are reported in great detail.

This complication is observed with sufficient frequency to warrant special consideration when obstruction occurs after laparotomy. The intussuscepta are confined to the small bowel and are rarely associated with rectal bleeding or a palpable abdominal mass. The development of vomiting and distention after the return of gastrointestinal function is characteristic. Roentgenograms usually show mechanical obstruction with intra-abdominal fluid. There is leukocytosis of marked degree.

In children, therapy by intraluminal suction in cases of apparent adynamic ileus or adhesive obstruction should be brief, with recognition of the fact that postoperative intussusception is a real entity and necessitates surgery. —*Eva S. Carey, M.D.*

Rajic, D. S. Some lesions of the colon in infancy and childhood. *Canad. M.A.J.*, Apr. 22, 1961, *84*, 880–886. (From: The Departments of Radiology, War Memorial Children's Hospital, London, Ontario, and the University of Western Ontario, Canada.)

The author discusses Hirschsprung's disease and intussusception of the bowel and emphasizes the contribution of the radiologist in the diagnosis and treatment of these conditions. He describes a new method of fluoroscopy with use of the image intensifier and points out that this is an excellent procedure for studying infants and young children. He feels that it eliminates most of the objections to treatment of intussusception by barium enema.

Hirschsprung's disease is also known as congenital megacolon and, recently, as aganglionic colon. Although the diagnosis is relatively simple it is frequently delayed or missed. The demonstration of a narrow segment of the distal colon and dilatation and hypertrophy of the colon proximal to the narrow segment are usually diagnostic of this condition. It is noted that the rectosigmoid area may be obscured in the plain posteroanterior study and, for this reason, it is felt that oblique roentgenograms of the rectosigmoid area must always be made to avoid missing a small area of aganglionosis. Occasionally a rectal biopsy is indicated in order to make the diagnosis more positive.

Intussusception is described and illustrated by several case reports. Reduction by barium enema is discussed in some detail and the advantages and disadvantages of this method are listed.

The statistics published by Ravitch of the Children's Hospital in Pittsburgh show no significant difference in mortality between the cases treated with barium enema and those treated surgically. The author believes that the reduction in radiation exposure, which can be accomplished by use of the image intensifier, removes the only remaining objection to the reduction of intussusception by barium enema.—*Richard E. Kinzer, M.D.*

Gasster, Marvin, Golden, Ross, Will, Drake, and Mellinkoff, Sherman M. Xanthomatosis involving the colon and small intestine. *Am. J. Digest. Dis.*, Apr., 1961, *6*, 312–321. (From: The Departments of Medicine, Radiology and Pathology, University of California School of Medicine, Los Angeles, Calif.)

This article reports a case of xanthomatosis of the colon in a fifty-four year old female who had been under observation because of induration and swelling of some areas of her skin. Over most of her body the skin was thickened and its color gave it the appearance of a pumpkin. She was intermittently anemic and the blood cholesterol ranged between 300 and 600 mg. per cent. She had chronic disease of the liver.

Mucous membranes of the soft palate and pharynx showed a deposition of yellowish-orange pigmentation. Pigmentation of the rectal mucosa was also noted on proctosigmoidoscopy. She ultimately became jaundiced and died in another hospital, death apparently being due to myocardial infarction, although this was not demonstrated at autopsy.

Barium enema examination of the colon is stated to have revealed variations in the mucosal pattern, but the roentgenograms reproduced in good illustrations are not very convincing. Small bowel changes are also described, but the autopsy record does not mention the small bowel. Microscopic sections from the colon show xanthoma cells in the submucosa only. Unfortunately, the autopsy findings were not correlated with the clinical history.—*Richard E. Kinzer, M.D.*

Crosta, Clemente, and Favero, Pier Alessandro. Sur les résultats obtenus avec l'examen tomographique dans l'étude des voies biliaires au moyen de la cholangiographie intraveineuse. (Results of laminagraphic examination in study of the bile ducts during intravenous cholangiography.) *Radiol. Clin.*, July, 1960, *29*, 224–250. (From:

Institut de Pathologie Chirurgicale de l'Université de Milan, Milan, Italy.)

Laminagraphic examination may be of considerable importance in cholangio-cholecystography. It is very useful for a clear demonstration of the bile ducts and occasionally it is helpful for better visualizing the gallbladder. Laminagraphy aids the examiner in determining more precisely when the biliary system is normal. Also, when pathologic changes are present, the details are more clearly shown.

Laminagrams are usually taken after about twenty minutes if the common bile duct is seen on a routine roentgenogram of the right upper quadrant. If very poor visualization is obtained, an injection of morphine or of other drugs which may cause relative contraction of the spincter of Oddi is given. Laminagrams are usually taken in slightly oblique positions with the first cuts at 7-8-9-10 cm. from the table top.

The results in 71 patients are tabulated and fifteen roentgenographic reproductions. are included.—*Charles M. Nice, Jr., M.D., Ph.D.*

Frimann-Dahl, J. Radiology in tumours of the pancreas. *Clin. Radiol.*, Apr., 1961, *12*, 73–79. (From: The Roentgen Department, Ulleval Hospital, Oslo, Norway.)

Of the intra-abdominal organs, the pancreas is one of the most difficult to examine. Its retroperitoneal position at the height of L2–L3 makes palpation of the normal gland nearly impossible and the close connection with the posterior abdominal wall prevents distinction from other organs.

There are mainly two types of tumors which occur in the pancreas—the carcinomas and the cysts. Clinically, carcinoma of the body of the pancreas produces continuous, severe pain, most pronounced when the patient is lying on his back and relieved when he is sitting up. Tumors of the head of the pancreas present with jaundice as the first sign, later associated with pain and vomiting.

In the last decade new methods of investigations have been developed which, to some degree, are superior to the conventional ones. Procedures for the direct or indirect diagnosis of tumors of the pancreas are: (1) conventional gastrointestinal study (including plain roentgenography); (2) pre-, inter- and postoperative cholangiography (using biligrafin); (3) pancreatography during or after operation (establishment of an external fistula and injection of contrast medium); (4) pneumolaminapancreatography (insufflation of retroperitoneal air and inflation of the stomach); (5) aortography (especially by the introduction of a catheter into the celiac artery); and (6) splenoportography.

In the diagnosis of carcinoma of the pancreas, various writers have stressed the demonstration in gastrointestinal studies of indentations or defects in the contour of the stomach or duodenum caused by the tumor and, in addition, changes in the mucosal pattern. Small defects and indentations occur first on the inside of the duodenal loop and in the pyloric region. In these areas they indicate a tumor of the head of the pancreas. The larger indentations on the stomach and colon, related to tumors of the body and tail of the pancreas, may represent either neoplasms, which are usually inoperable, or benign tumors, such as cysts and pseudocysts.

At operative cholangiography, coincident filling of the pancreatic duct for its entire length may occur. Indentation, displacement or deformity of the common duct may indicate the presence of a pancreatic tumor.

A method of pancreatography performed during operation was described by Leger, Gally and Arvay in 1954. Another technique was reported by Macarini and Perassi in 1953. They used a combination of retroperitoneal insufflation, gas in the stomach and transverse axial laminagraphy, making it possible for the first time to see the pancreas directly. If properly done, it is easily performed and safe for the patient. Laminagrams are taken either in the horizontal position, with the patient in lateral recumbency, or in the erect lateral position, and transverse sections are made with the patient sitting or standing upright. In the lateral position, several laminagrams must be taken to include the area from the head to the tail of the pancreas. The gland is then seen to be "floating" in the retroperitoneal air in front of the kidney, bordered anteriorly by the gas-distended stomach. Transverse axial laminagrams are more difficult to obtain and also more difficult to interpret. This is particularly true in thick, heavy individuals. Such studies are often decisive for final diagnosis. In normal cases the retroperitoneal air seems quite regularly to "dissect out" the pancreas, so that the contours are well shown and the gland "floats" in the air. In pathologic cases, when the pancreas is not clearly outlined, the blurred contours may indicate a lesion with some degree of certainty.

Angiography is a valuable aid in studying tumors of the pancreas. Aortography is, in many ways, nearly as effective and may even be better than using selective injection into the celiac artery, because of a simultaneous filling of other vessels. Amundsen has pointed out that downward displacement of the kidney, indicated by a steeper angle of the renal artery, is often noted with tumors of the pancreas. The renal or hepatic artery may be bent caudally, and the aorta is often curved more to the left than normal. When a patient with an aneurysm of the abdominal aorta is admitted with a diagnosis of pancreatic tumor, the aneurysm will probably be overlooked if the examination is limited to injection of the celiac artery, but aortography will reveal the dilated vessel. However, a lateral view is one of the advantages of the selective method, and such a view can hardly be obtained in aortography. Also, by using splenoportography, information can be gained about the pres-

ence of a pancreatic tumor, for instance, by showing invasion of the splenic or hepatic vein.

In summary, the author feels that retroperitoneal insufflation of oxygen combined with laminagraphy is particularly valuable in the diagnosis of tumors of the pancreas.—*Samuel G. Henderson, M.D.*

Gynecology and Obstetrics

Bennett, M. F., Lynch, J., and Tweedie, F. J. The erect lateral projection of the pelvis: an assessment of its value as an initial procedure in pelvimetry. *J. Canad. A. Radiologists*, Mar., 1961, *12*, 10–14. (From: The Royal Victoria Hospital, Montreal, Quebec, Canada.)

The authors studied the erect lateral roentgenograms of the pelvis in 317 patients examined in the Royal Victoria Hospital between 1954 and 1958 in an attempt to determine the percentage in whom a vaginal delivery could be predicted. The shortest anteroposterior diameters of the inlet and of the outlet were measured. The shape and inclination of the sacrum, the width of the sacrosciatic notch and the relationship to the presenting part were evaluated. Cephalometry was done when possible.

In a group of 278 cases, uncomplicated vaginal delivery was predicted in 189. This proved to be correct in 181 cases, an accuracy of 95.8 per cent. The error was primarily due to failure to recognize lower pelvic strait disproportion.

The main advantage of this single roentgenogram technique is the reduction in the radiation exposure of the maternal ovaries and of the fetus. The principal deficiencies are related to the impossibility of determining the interspinous diameter and the pelvic shape.—*J. N. Ané, M.D.*

Baghdassarian, Olga M., Koehler, P. Ruben and Schultze, Gunter. Massive neonatal ascites. *Radiology*, Apr., 1961, *76*, 586–592. (Address: O. M. Baghdassarian, Johns Hopkins Hospital, Baltimore 5, Md.)

The authors review the literature of massive fetal or neonatal ascites and present 3 cases of this rare intraperitoneal accumulation of fluid during prenatal life or shortly after birth. Three large groups of underlying anatomic abnormalities have been implicated in the pathogenesis of this condition: (a) intestinal anomalies such as perforation of the bowel secondary to malformation; (b) portohepatic abnormalities producing obstruction of the portal circulation; and (c) anomalies of the lower urinary tract.

The accumulation of large amounts of fluid in gastrointestinal abnormalities is usually the result of perforation of a viscus secondary to atresia, stenosis, intussusception, volvulus, or herniation. Portohepatic abnormalities produce ascites through intra- and/or extrahepatic obstruction of portal circulation, and are rarely amenable to surgery. Intrahepatic obstruction is the more common and is due to congenital hepatic cirrhosis. Genitourinary abnormalities are associated with atresia of the urethra or urethral obstruction. The method of fluid formation intraperitoneally in urethral obstruction is not clear except in cases of perforation of the bladder, but it may be due to transudation.

Roentgenographically, there is diffuse, homogeneous opacification of the abdomen, with bulging flanks and lack of properitoneal fat lines. When bladder neck obstruction is present, the cystourethrogram is usually diagnostic. The authors stress that neonatal ascites not associated with generalized edema is an emergency situation with a grave prognosis, unless there is prompt correction of the underlying congenital anomaly.—*John S. Alexander, M.D.*

Blood and Lymph System

Boller, R., and Deimer, E. Die perkutane Splenoportographie und der intrasplenale Adrenalintest bei der Leberzirrhose. (Percutaneous splenoportography and the intrasplenic adrenalin test in cirrhosis of the liver.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Feb., 1961, *94*, 199–207. (From: Medizinische Abteilung des Allgemeinen Krankenhauses in Wien, Vienna, Austria.)

The authors examined 114 patients for hepatic diseases and used as diagnostic criteria the vertical diameter of the spleen on the roentgenogram, intrasplenic pressure values (both before and after intrasplenic injection of adrenalin), evidence of functional and anatomic alterations in the portal venous system, and, finally, the intrasplenic adrenalin test.

The following procedure was employed: A laparoscopic examination is made, which yields valuable macroscopic and microscopic information and permits insertion of a needle into the hilus of the spleen. A pressure gauge is connected to the needle and the intrasplenic pressure is determined. Roentgenograms are made during and after injection of from 40 to 60 ml. of contrast medium. Then, 1/10 mg. of adrenalin is injected into the spleen and the intrasplenic pressures are continuously recorded. At the same time the peripheral blood pressures are determined.

Great splenic enlargement was observed in cases of acute hepatitis and in advanced cirrhosis. In chronic hepatitis and in early cirrhosis, the size of the spleen remained essentially normal.

The intrasplenic pressure was slightly below the portal pressure in normal persons, as well as in patients with fatty degeneration or atrophy of the liver. In inflammatory hepatic diseases and in cirrhosis, the intrasplenic pressures were greatly increased unless there was collateral circulation between the portal and the caval systems.

The observations after intrasplenic injection of adrenalin were as follows: In the normal patient the spleen contracted and the intrasplenic pressure increased by approximately 200 mm. of water. The peripheral blood pressure remained unchanged. Patients with severe cirrhosis, on the other hand, showed increases of only 100 mm., or even negative values. In the presence of portacaval collateral circulation, the increase in intrasplenic pressure was insignificant, but the peripheral blood pressure rose within one minute after the injection of adrenalin.

The authors inject 60 ml. of 76 per cent urografin within six seconds. If the injection of the contrast medium is too forceful and too fast, retrograde filling of the veins occurs, simulating pathologic portacaval collateral circulation. It is of special importance to realize that in those cases the intrasplenic adrenalin test will not result in an elevation of the peripheral blood pressure.—*Wolfgang H. Steinmetz, M.D.*

Vargas, Lester L., and Forsythe, Thomas. A syringe heater for angiocardiography. *Radiology*, Feb., 1961, *76*, 248–250. (Address: Rhode Island Hospital, Providence 2, R. I.)

The authors describe a syringe heater which they designed for use with a mechanical injector. Its purpose is to maintain the radiopaque medium used for angiocardiography at body temperature before and during the injection. This is essential when 90 per cent diatrizoate (hypaque) is used, because this preparation has the disadvantage of separating into crystalline and fluid fractions at room temperature.

The syringe heating device consists of a hollow cylinder, machined from a standard rod of stock aluminum, which fits around a Lehman 50 cc. syringe. A slot along one side permits visualization of the calibrations on the syringe. A copper electrical thermal immersion element supplies the heat by conduction to the aluminum jacket. The solution reaches body temperature in ten to fifteen minutes and the temperature is maintained at that level by a thermostat. The advantages of this heater are its simplicity and its low cost.—*W. M. McBride, M.D.*

Wallace, Sidney, Jackson, Laird, Schaffer, Burton, Gould, John, Greening, Roy R., Weiss, Arthur, and Kramer, Simon. Lymphangiograms: their diagnostic and therapeutic potential. *Radiology*, Feb., 1961, *76*, 179–199. (Address: Department of Radiology, Jefferson Medical College Hospital, Philadelphia 7, Pa.)

A modification of Kinmonth's method of intralymphatic injection was used to demonstrate the lymphatics and lymph nodes of the extremities, including the pelvic, para-aortic, axillary, and supraclavicular areas, as well as the thoracic duct. A mixture containing equal parts of 0.5 per cent Evans blue dye and 1 per cent procaine hydrochloride was injected intradermally into the interdigital web space between the first and second digits to make the lymphatic channels identifiable. Ethiodol was injected slowly into the exposed lymph vessel without undue pressure. Five to 7 ml. of radiopaque material was used for studies of the upper extremity and 10 to 15 ml. in the lower extremity. Roentgenograms were taken at the completion of the injection and again twenty-four hours later. The lymph nodes were best seen on twenty-four hour roentgenograms.

This report presents the results in the lymphangiographic study of 110 patients; 207 extremities were injected (174 lower and 33 upper). The lesions studied were as follows: carcinoma, 54; lymphoma, 28; edema, 12; infection, 5; and miscellaneous, 11. Complications were infrequent and not serious. Two patients experienced transient lymphangitis. Frank wound infection occurred three times.

In lymphedema, the findings varied from an increase to an almost complete absence of channels. Extensive collateral pathways were demonstrated in the presence of obstruction to lymph flow. The normal lymph nodes have a homogeneous reticular pattern. In lymphadenitis, the lymph nodes are larger but normal in architecture; in lymphomas they are enlarged, lacy, and ghost-like; in carcinoma the lymph nodes have a moth-eaten appearance.

Lymphangiography can be used to determine the general type and extent of disease processes; as a guide to lymph node dissection; in radiation therapy for accurate portal placement; and in both radiation therapy and chemotherapy to assess the response to treatment.—*Arno W. Sommer, M.D.*

RADIATION THERAPY

Buttenberg, Dietrich, Schönfelder, Ruth, and Stoll, Peter. Zur Prognose der Strahlentherapie des Kollumkarzinoms nach der "Sensitization Response." ("Sensitization response" in the prognosis of radiation therapy for carcinoma of the cervix.) *Strahlentherapie*, Dec., 1960, *113*, 538–552. (From: Universitäts-Frauenklinik, Heidelberg, Germany.)

In the vaginal smears of 128 patients with carcinoma of the cervix followed during radiation therapy, 44 (34.4 per cent) showed distinct "sensitization response" (Graham), and 84 (65.6 per cent) showed only slight "sensitization response." From two and one-half to five years after therapy, 28 (63.6 per cent) of the patients who had distinct "sensitization response" and 51 (60.7 per cent) of those who had had slight "sensitization response" were free of signs and symptoms of carcinoma of the cervix.

Because of this insignificant difference between

the two groups, the authors have dismissed "sensitization response" as a valid basis for prognosis of the effectiveness of radiation therapy for carcinoma of the cervix.—*Henry G. Moehring, M.D.*

Kolling, Hans-Lothar, and Reuter, Ernst. Strahlenbelastung und Strahlenschutz der menschlichen Linse bei therapeutischen Massnahmen in Augennähe. (Radiation exposure and protection of the human lens in therapy about the eye.) *Strahlentherapie*, Oct., 1960, *113*, 299–311. (From: Institut für Röntgenologie und Strahlenkunde der Universität, Jena, Germany.)

On the basis of measurements in air with various eye shields and in both infant and adult sized phantoms, the authors arrived at the following conclusions in regard to radiation therapy about the eye (their specific concern was treatment of hemangiomas):

(1) To offer protection of consequence, eye shields should fit the bulb and should be made of high lead content glass or, better yet, of approximately 2 mm. of metallic lead.

(2) With radium molds applied anteriorly, even the best lead shields which were tested reduced the irradiation of the lens by only one-third. Eye shields failed to protect the lens from radiation when radium molds were applied about the eye other than anteriorly.

(3) Eye shields can reduce irradiation of the lens by about one-half when interstitial radium is used, particularly when the needles are applied in the lids. Much of this protection results from increasing the distance between the lens and the radium sources.

(4) Treatment of hemangiomas in the region of the eye with contact roentgen therapy and with the eye protected by suitable, effective eye shields exposes the lens to the least radiation hazard.—*Henry G. Moehring, M.D.*

Pohlit, Wolfgang. Die Messung der Neutronenstreustrahlung an einem 35 MeV-Betatron. (Measurement of stray neutrons from a 35 mev. betatron.) *Strahlentherapie*, Nov., 1960, *113*, 469–474. (From: Max-Planck-Institut für Biophysik, Frankfurt/Main, Germany.)

The author diagrams the levels of slow and fast neutron flux around a 35 mev. betatron in a treatment room. He measured slow neutrons with indium foil and fast neutrons with indium foil encased in paraffin cylinders of 12 cm. diameter.

Of the secondary radiations around a betatron operating at more than 20 mev., the bremstrahlung and neutron radiation have approximately equal import (in the range of mrem per hour) for personnel; for the patient, bremstrahlung is more important (1–2 per cent of the primary dose), though neutrons play an equally important role in secondary radiation to the eyes. Radiation activity produced in the ambient air is negligible for both personnel and patient; its maximum is 0.01 per cent of the primary dose.—*Henry G. Moehring, M.D.*

Westfall, Michael P. Radiation nephritis in adults and children; effects of radiation on growing bones. *J. Urol.*, Apr., 1961, *85*, 476–482. (From: The Veterans Administration Hospital, Bronx 68, N. Y.)

In this article, the author bases his findings and recommendations upon a review of 66 adult patients with testicular tumors who were irradiated over the renal area and 15 patients in the younger age group who were irradiated for Wilms' tumor. Of the 66 patients who were irradiated for tumor of the testis, 23 developed urinary tract signs and symptoms suggestive of nephritis; of the 15 patients with Wilms' tumor, 5 developed albuminuria or casts following irradiation of the involved kidney or renal fossa.

Two of the children who were irradiated for Wilms' tumor showed evidence of interference with bone growth—hemivertebral atrophy of the lumbar spine in 1 and arrested growth of the iliac bone in the other.

The author includes a historical survey of other reports of similar radiation damage. His experience is another example of the well-known fact that irradiation will produce damage to normal tissues when given in large amounts and over a long enough period of time. It is unfortunate that the author does not give more specific data regarding the quality and quantity of radiation, and the time factors involved in the production of the changes which he reports.—*George W. Chamberlin, M.D.*

Baudisch, Eberhard. Beitrag zu den Strahlenschäden der Rippen und Schlüsselbeine bei Brustkrebs-Patienten. (Radiation damage to the ribs and clavicles in patients with carcinoma of the breast.) *Strahlentherapie*, Oct., 1960, *113*, 312–318. (From: Institut für Röntgenologie und Strahlenkunde der Universität, Jena, Germany.)

Of 369 patients with cancer of the breast irradiated between 1950 and 1955, 4 developed spontaneous fractures of the ribs and clavicle attributed to radionecrosis. The author agrees with previous reports that doses of 1,800–4,000 r can produce such spontaneous fractures and that they may appear as early as twelve months after irradiation. Clinically, these fractures tend to be silent and to be discovered on follow-up chest roentgenograms.—*Henry G. Moehring, M.D.*

RADIOISOTOPES

Walfish, Paul G., Britton, Amy, Volpe, Robert, and Ezrin, Calvin. Experience with an *in vitro* test of thyroid function—the red blood cell uptake of L-triiodothyronine labelled with radioactive iodine. *Canad. M. A. J.*, Mar. 25, 1961, *84*, 637–641. (From: Departments of Medicine and Pathological Chemistry of the University of Toronto and the Clinical Investigation Units of Sunnybrook (D.V.A.) and Toronto General Hospitals, Toronto, Ontario, Canada.)

While the technical procedures of this test are directed at determining the radioactivity of washed erythrocytes following incubation with T_3-I^{131} and calculating the percentage uptake, it is felt that the test really measures indirectly the ability of certain unsaturated plasma proteins to bind added T_3-I^{131}.

In this study, 240 determinations of the R.C.U. (red cell uptake) of T_3-I^{131}, performed according to the method of Hamolsky *et al.*, revealed that 89 per cent in the euthyroid group were within the range of 12.5–18.5 per cent uptake. Eighty-three per cent of the hyperthyroid group had greater than 18.5 per cent uptake with all the normal R.C.U. values occurring in the untreated nodular and previously treated diffuse thyrotoxic patients. In the hypothyroid group, 77 per cent had less than 12.5 per cent uptake; three quarters of those with normal R.C.U. values had recently received thyroid hormone therapy. For the most accurate and reproducible results, the authors recommend that the test be performed on the blood within twenty-four hours of sampling and that silicone glassware be used throughout.

The chief advantages of the R.C.U. test over other tests of thyroid function are: (1) it is not significantly influenced by iodine contamination; (2) it avoids the administration of a radioactive material to the patient; (3) it measures another aspect of thyroid physiology.

Clinical factors which reportedly have no significant effect on the R.C.U. result are colloid and nontoxic nodular goiters, thyroid carcinoma, exogenous iodine, anxiety, congestive heart failure (without hepatic failure), hypertension, administrations of mercury, and some endocrinopathies.

A significant decrease in the R.C.U. has been demonstrated during normal pregnancy, functional hyperestrogen states, and propylthiouracil or iodine therapy for hyperthyroidism.

A significant increase in the R.C.U. may occur if the patient is taking anticoagulants, or is suffering from renal disease (especially nephrosis), severe liver disease, severe metastatic malignancy, severe pulmonary insufficiency, paroxysmal atrial arrhythmias, or polycythemia rubra vera.

An addendum to the article reviews a newly published method of calculating an improved hematocrit correction for use in this test. This new method is most valuable when the hematocrit is outside the 30–40 per cent range.—*Donald M. Monson, M.D.*

Rosenthall, Leonard. A rapid screening method for I^{131} fat-absorption test. *Radiology*, Feb., 1961, *76*, 251–254. (Address: Ontario Cancer Institute, Princess Margaret Hospital, 500 Sherbourne Street, Toronto 5, Ontario, Canada.)

The usual method for determining small bowel absorbability of an oral test dose of I^{131} tagged triolein is to take blood samples at three, four, five, and six hours after ingestion. The total blood activity is then compared with normal values. The author states that, with oral doses of about 20 μc, enough activity was present at the end of three hours to be counted by means of a scintillation detector probe placed against the head. A linear relationship was found to exist between the number of microcuries in the blood and the head counts. The examination is terminated in patients having normal head counts at the end of three hours, while venipuncture is done as usual with those patients whose head counts indicate a low activity.

The author presents details of his study in determining normal head counts in 32 patients. After three hours the relationship is not accurate, as iodine is deposited in the brain. The exact relationships must be determined by the individual laboratory.—*James C. Moore, M.D.*

Wagner, Henry N., Jr., McAfee, John G., and Mozley, James M. Diagnosis of liver disease by radioisotope scanning. *A.M.A. Arch. Int. Med.*, Mar., 1961, *107*, 324–334. (From: Diagnostic Radioisotope Laboratory, Johns Hopkins Hospital, Baltimore, Md.)

The authors use an automatic photoscanning device (which records on x-ray film) to detect and evaluate suspected diseases in the upper quadrant of the abdomen. The patient is given 100 μc of either rose bengal or colloidal radioactive gold intravenously. The scan film is superimposed on an anteroposterior supine roentgenogram of the patient's abdomen and lower chest. The authors demonstrate in 19 different figures how these composite pictures can aid in the diagnosis of upper abdominal disease.

This article also illustrates how the demonstration of filling defects in the liver has aided in the diagnosis of pyelogenic abscess of the liver, amebiasis, primary and metastatic tumor from the liver, and vascular anomalies. The position of the liver has helped in the detection of a subphrenic abscess and congenital malposition of the liver, and it has served to differentiate lower lobe pneumonias from sub-

phrenic abscesses. The authors demonstrate how they use this technique for the differential diagnosis of abdominal masses, for differentiation between obstruction and parenchymal liver disease, and for preoperative evaluation of patients with suspected liver malignancies. In addition, they illustrate the use of this technique in demonstrating Riedel's lobe of the liver, in localizing therapy ports, in evaluating the effect of chemotherapy on liver metastasis and in differentiating between mild and severe infectious hepatitis.

If the necessary equipment is available the technique is fast and simple; it is easy for the operator to perform and for the patient to undergo. The radiation dose is less than that from routine roentgen studies, except in the case of a patient with complete biliary obstruction. Therefore, this procedure is another practical and effective aid to the physician trying to make a definitive diagnosis in suspected disease of the uper abdomen.—*William W. Joule, M.D.*

Frost, Dietrich, and Werkes, Heinz. Über ein neues Verfahren zur Darstellung schwach speichernder Gewebe in der Gamma-Szintigraphie. (A new arrangement for gamma-scintigraphic delineation of tissues with relatively low uptake.) *Strahlentherapie*, Nov., 1960, *113*, 461–468. (From: Abteilung für Strahlungsphysik des Städt. Rudolf-Virchow-Krankenhauses Berlin and Entwicklungsabteilung der Dr. H. Stamm K. G., Berlin, Germany.)

Scintigraphic and photogammagraphic distinction between normal and abnormal tissues, when the differential uptake of radioactive material is slight, depends on suppressing background signals (which arise from the surrounding "normal" tissues) and then improving contrast between the useful signals by steepening the differential curve between impulse rates from the "abnormal" tissue and from its edges.—*Henry G. Moehring, M.D.*

Bogasch, U., Käsbauer, H., and Künlen, H. Erfahrungen mit der Radiogoldspickung der Hypophyse bei metastasierenden Neoplasmen unter besonderer Berücksichtigung des Mammakarzinoms. (Experiences with radiogold seeding of the hypophysis in metastasizing neoplasms with special consideration of mammary carcinoma.) *München. med. Wchnschr.*, Jan., 1961, *103*, 147–150. (From: Chirurgische Abteilung des Städt. Krankenhauses München r. d. Isar and Strahlenabteilung des Städt. Krankenhauses München r. d. Isar, Germany.)

Sex hormones influence the growth and function of glandular carcinoma, especially of the breast. The aim of therapy, therefore, is to eliminate the follicular hormone. Administration of male hormones only impairs but does not suppress the formation of estrogen. Ovariectomy is of temporary benefit because the hyperplastic adrenal cortex soon starts producing steroids.

Suppression of the pituitary hormone remains as the most effective approach since this causes atrophy of the adrenal cortex and of the ovary. Removal of the hypophysis is compatible with life, although prolactine and the growth hormone are eliminated.

Surgical extirpation of the gland is associated with a high mortality. Electrocoagulation is not reliable and roentgen therapy is inadequate. Therefore, the application of radioactive isotopes has become the method of choice. The authors prefer radiogold to the yttrium isotope and injection via a percutaneous rather than a transnasal route. To prevent damage to the optic nerves and other vital structures, the dosage is kept to a minimum of three seeds of Au^{198} (10 mc each).

Forty-eight patients were treated in the past four years: 35 cancers of the breast, 10 of the ovary, 2 of the cervix and 1 of the colon. The results were disappointing in tumors of the ovary, uterus, and colon.

Criteria for remission were general improvement and regression of metastases for at least one year. There were only 2 definite remissions with the disappearance of metastatic nodes and filling in of osteolytic foci. The 2 cases are illustrated by serial roentgenograms taken over a period of several years. Two-thirds of the patients improved subjectively and one-third was not influenced.

Spontaneous remissions may occasionally occur in similar far advanced cases, but the results in the cited 2 patients were so impressive that the authors extended the indication for hypophyseal sterilization to less advanced cases Thus, they hope that their final statistical results will compare favorably with those of other investigators.

There was no primary mortality due to the treatment. Transient postoperative headache, which was frequently observed, responded to sodium chloride infusions and vitamin medication. As to side effects, there were single cases of diabetes insipidus, retrobulbar hematoma, paresis of an oculomotor nerve, and 3 cases with transient fistulae of cerebrospinal fluid.

A special advantage of radiogold seeding is the fact that the operation can be repeated if necessary. There is no age limit, as proved by 2 patients who were seventy-five years old. The method, however, is contraindicated in terminal cases with metastatic involvement of the liver, lungs, and brain.—*Ernest Kraft, M.D.*

Miscellaneous

Stewart, Alice. Aetiology of childhood malignancies; congenitally determined leukaemias. *Brit. M. J.*, Feb. 18, 1961, *1*, 452–460. (Address: Dr. Alice Stewart, Reader in Social Medicine, Oxford University, Oxford, England.)

The survey data which first suggested that prenatal roentgen-ray exposure increased the risk of childhood malignancies also showed that leukemia is exceptionally common among mongoloids (Stewart, Webb, Hewitt, 1958) with the implication that for some cases of leukemia the decisive event dated back to the onset of mongolism.

The Rous theory of cocarcinogenesis assumes two stages in the development of cancers (Rous and Kidd, 1941)—"initiation" and "promotion." If this idea were applied to the concept of gene mutations, the sequence of events might be as follows. "Initiators" cause a mutation within a germinal cell but this remains silent until fertilization, when one of four things should occur: (1) miscarriage; (2) cancer development *in utero* or after birth; (3) development of premalignant disease (*e.g.*, intestinal polyposis); or (4) a normal phenotype with an abnormal genotype.

These ideas have been incorporated in the working hypothesis for childhood malignancies:

(1) Malignant diseases are "initiated" by roentgen rays and other mutagens before conception (prezygotic), during pregnancy (postzygotic) or after birth.
(2) In childhood, the chief promoter is the cell stress of embryogenesis; therefore, most cancers and leukemias are prezygotic.
(3) At all ages, infection stresses the leukocyte and promotes leukemia. Mongoloids have increased susceptibility to infection so mongolism indirectly promotes leukemia. Because mongolism is inherited, it is more likely to affect prezygotic than postzygotic leukemias.
(4) Prezygotic carcinomas and leukemias favor primitive cell types and may have familial incidence. Postzygotic carcinomas and leukemias favor mature cell types and have no familial incidence.
(5) No normal leukocytes are present in individuals with prezygotic leukemias, so there is exceptionally low resistance to infection.
(6) Recent increases in childhood leukemias reflect a falling death rate for pneumonias and infection and are due to prezygotic leukemias.

Two types of childhood leukemia are identified: (1) The more common variety of leukemia with lymphoblasts or monoblasts is derived from stem and blast cells. These cases (most frequently boys—frequently familial—often mongoloids) are prone to infection. It is postulated that prezygotic leukemias are due to a gene inheritance which produces premalignant changes in ancestral cells of the reticuloendothelial system. During embryogenesis further changes occur in these abnormal cells leading to malignancy. If the abnormal cell survives embryogenesis, it may become malignant under subsequent leukocyte stress, such as infection, or remain indefinitely in a premalignant stage. (2) In postzygotic leukemias, the cells may be myeloblasts, lymphoblasts or stem cells. These cases are not associated with mongolism, have no familial incidence, and are less susceptible to infection than those in the first category. It is postulated that these leukemias are due to changes in premalignant somatic cells. The unaffected leukocytes in these children behave normally during infection.

The final conclusion is that the role of leukocytes in pyogenic infections and the profound changes following the use of antibiotics have led to a discovery of a leukemia variety in which the first event predates conception and produces a preleukemic gene. The prezygotic leukemias derived from these genes are responsible for the early peak of leukemia mortality (two to four years) and have their counterpart in other cancers. It is also suggested that in any population the numbers of preleukemic genes and the number of prezygotic leukemias are to a large extent controlled by the prevalence of and mortality from pyogenic infections.—*Bernard Loitman, M.D.*



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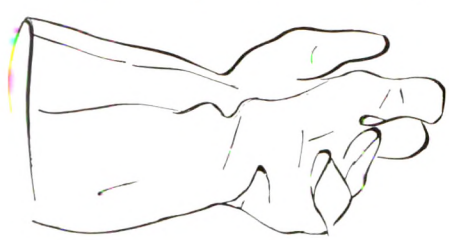
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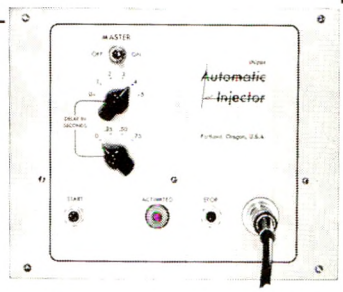
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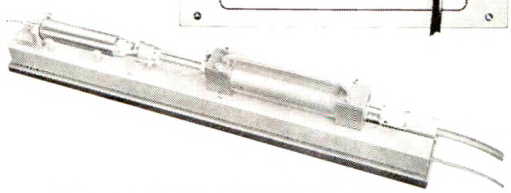
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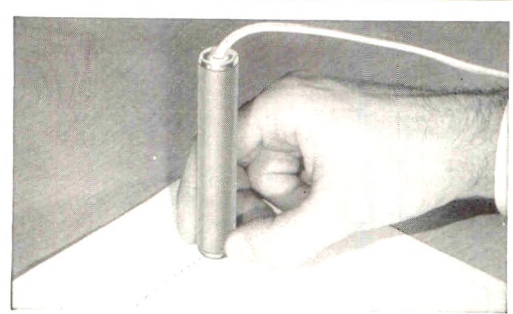
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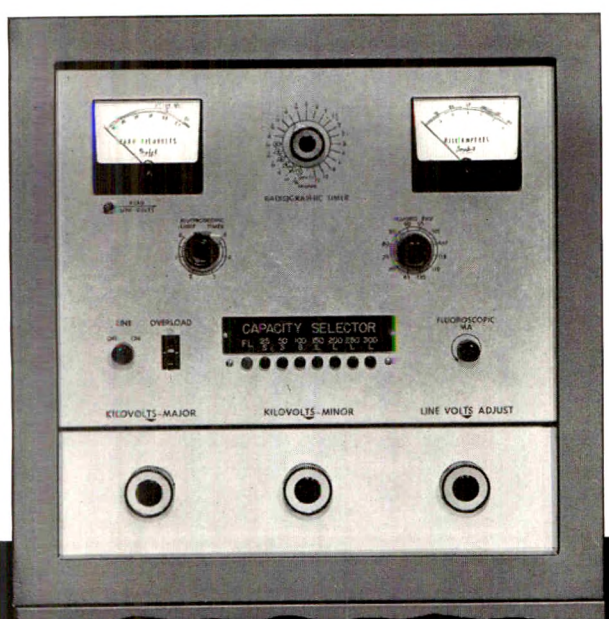
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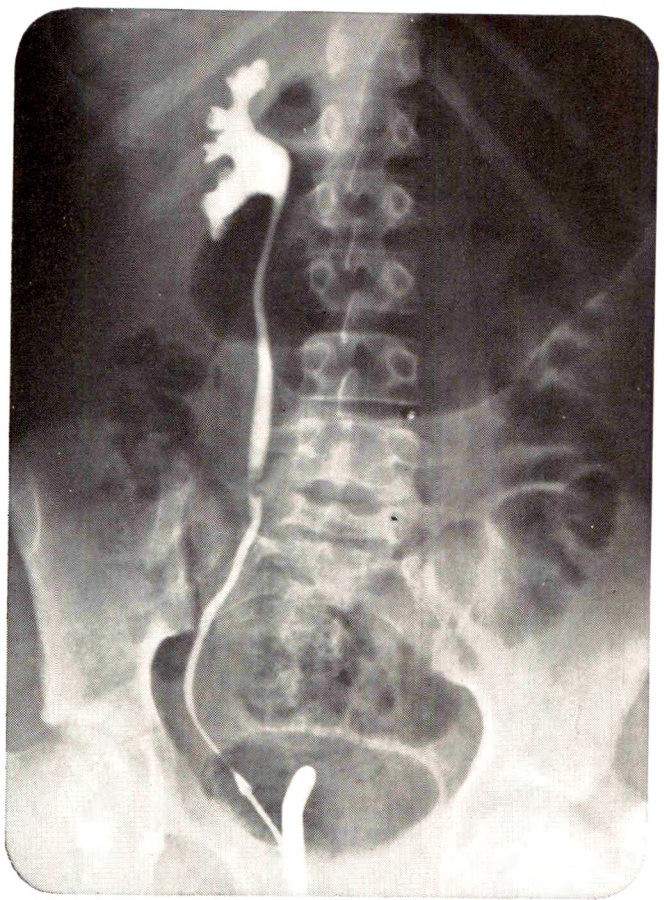
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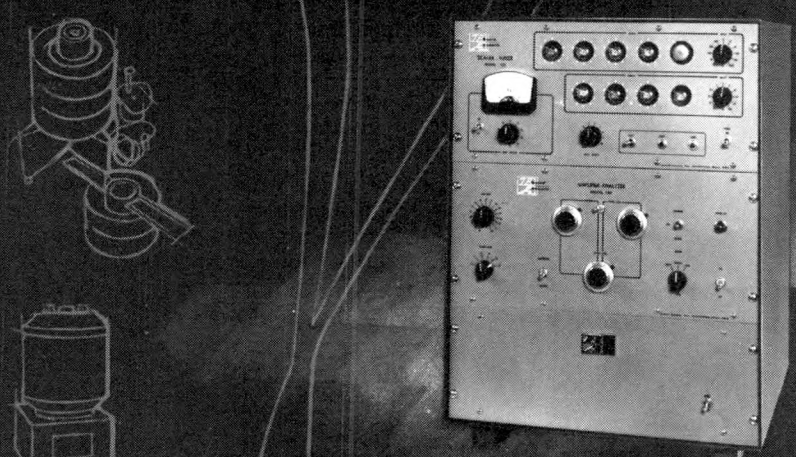
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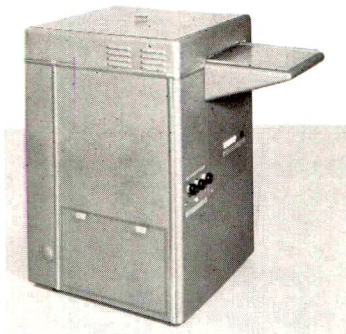
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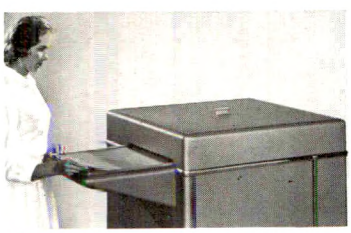
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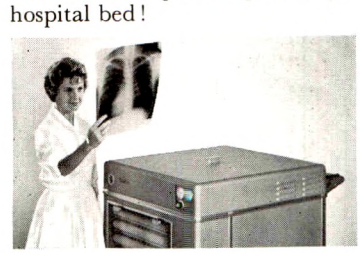
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RADIOGRAPHY OF INFANTS AND CHILDREN. *By* **Donald B. Darling,** *Univ. of Pittsburgh. With the Technical Assistance of James M. Anthony, Children's Hosp. of Pittsburgh.* With the increasing use of x-ray procedures in the pediatric age group and the rising emphasis on hazards of radiation to the general population, it is important to make use of pediatric x-ray techniques in which only the patient is exposed during examination and in which this exposure is minimal. THE TECHNIQUES SET FORTH IN THIS BOOK ANSWER BOTH OF THESE REQUIREMENTS. The main section of the text is divided into separate discussions on the infant and older child since the techniques used differ considerably. A separate chapter is devoted to the equipment needed and its general application. *The more specific use of the equipment is indicated under each individual examination.* A detailed discussion of radiation protection is presented in Chapter 2. A summary of suggested exposure factors is given in the appendix. *Pub. Jan. '62 (Amer. Lec. Roentgen Diagnosis).*

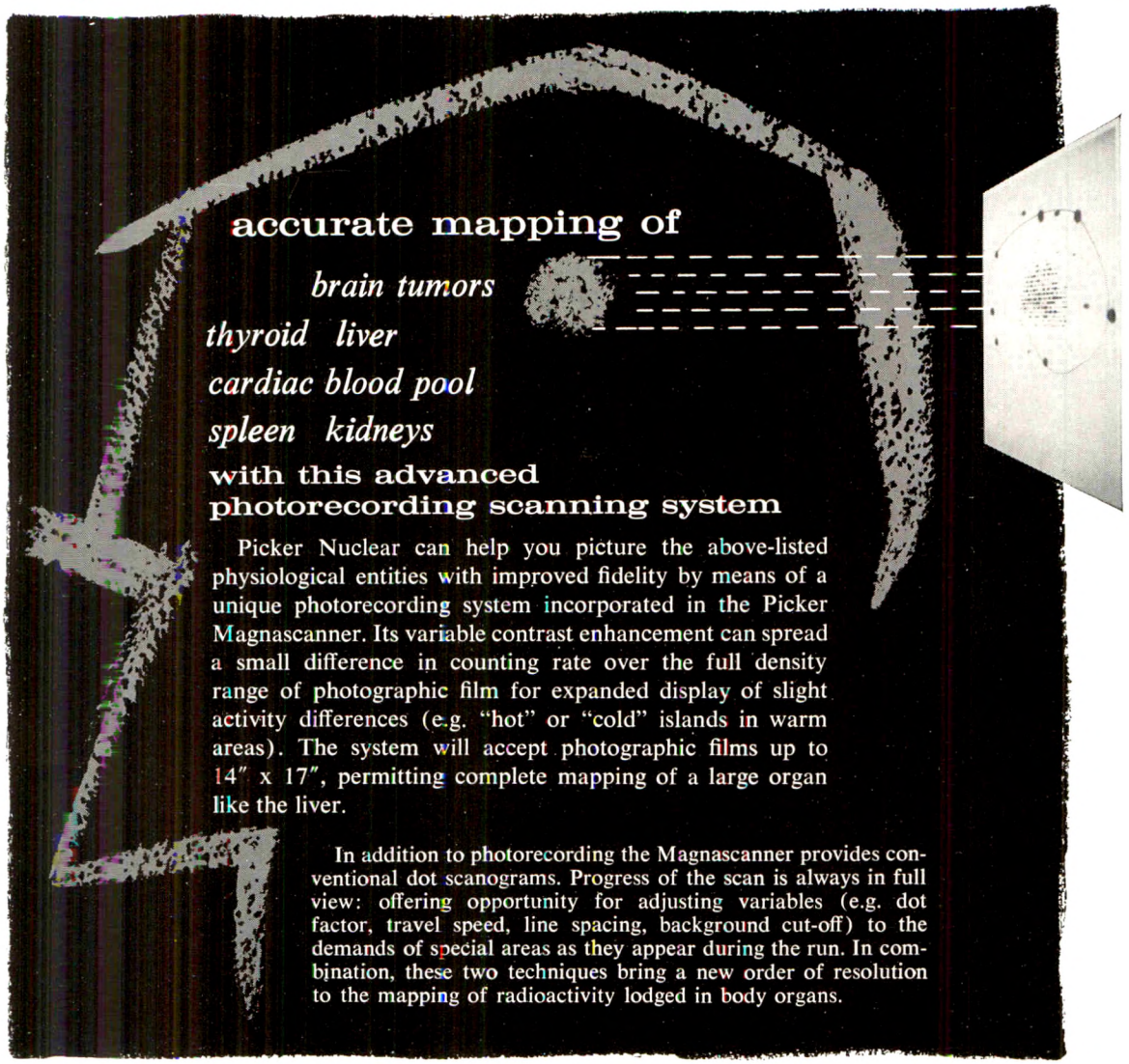
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AN ATLAS OF DETAILED NORMAL PNEUMOENCEPHALOGRAPHIC ANATOMY. *By* **Giovanni Di Chiro,** *National Institute of Health, Bethesda, Maryland.* For use in everyday diagnostic work—a detailed roentgenographic demonstration "in vivo" of intracranial structures. A *three-dimensional concept* of various anatomic formations is attained by their demonstration in lateral and sagittal roentgenograms. Lateral and coronal laminagrams, including laminagrams of the cerebrospinal fluid cavities of the posterior fossa, are illustrated. *A new technique of laminagraphy* combined with fractional encephalography, already tested in a large group of patients, is discussed. Emphasis is placed on demonstration of structures with less well known pneumoencephalographic appearance. *Some structures are demonstrated roentgenographically "in vivo" for the first time.* ABOUT 300 REPRODUCTIONS OF THE SAME SIZE AS THE ORIGINAL ENCEPHALOGRAMS AND AN ALMOST EQUAL NUMBER OF EXPLANATORY SKETCHES ARE INCLUDED. *Pub. Aug. '61, 352 pp. (11 × 8½), 515 il. (4 in full color), $19.00.*

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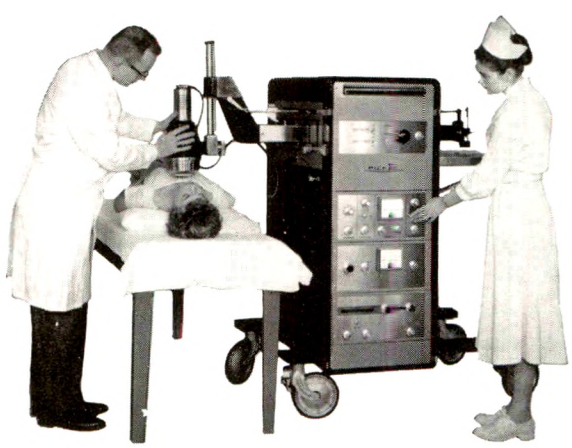
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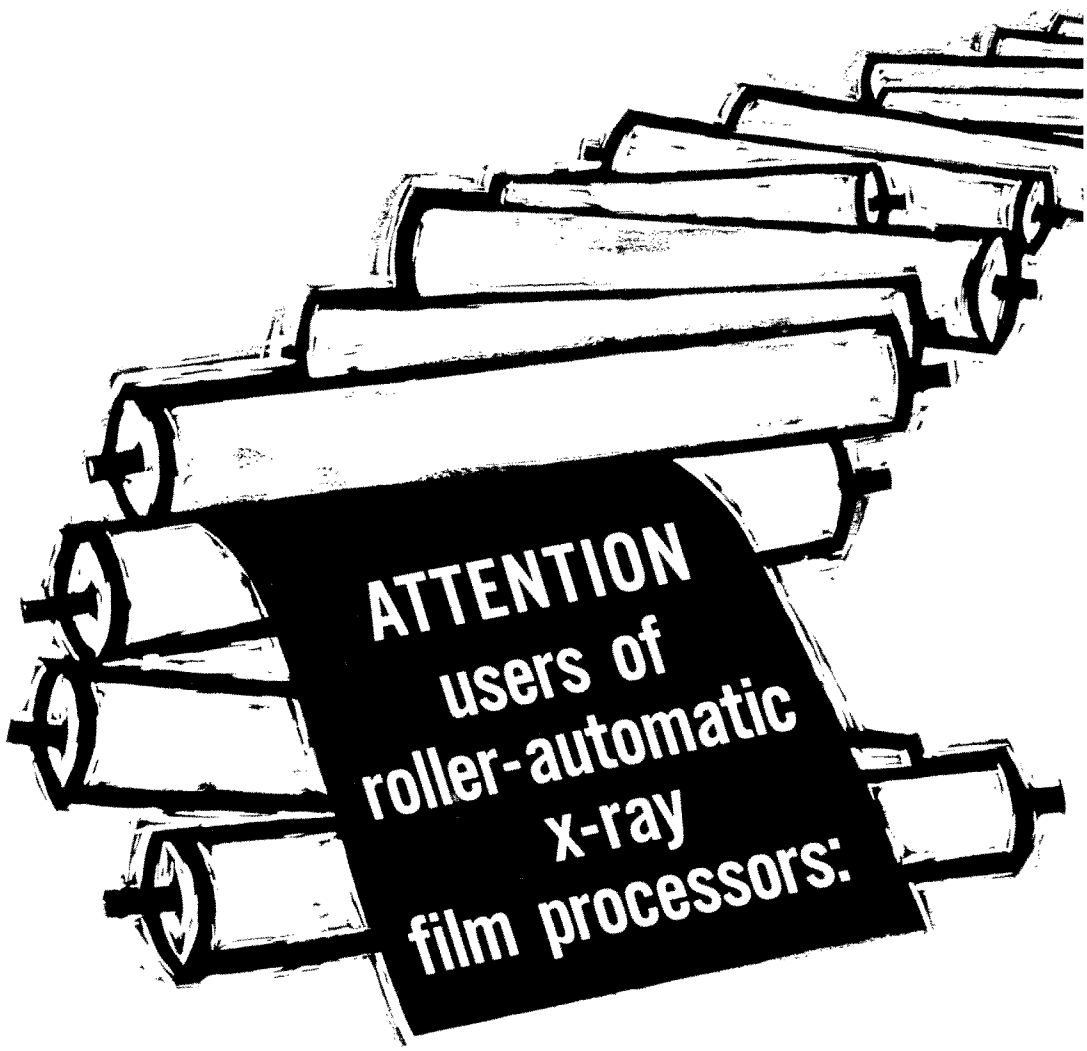
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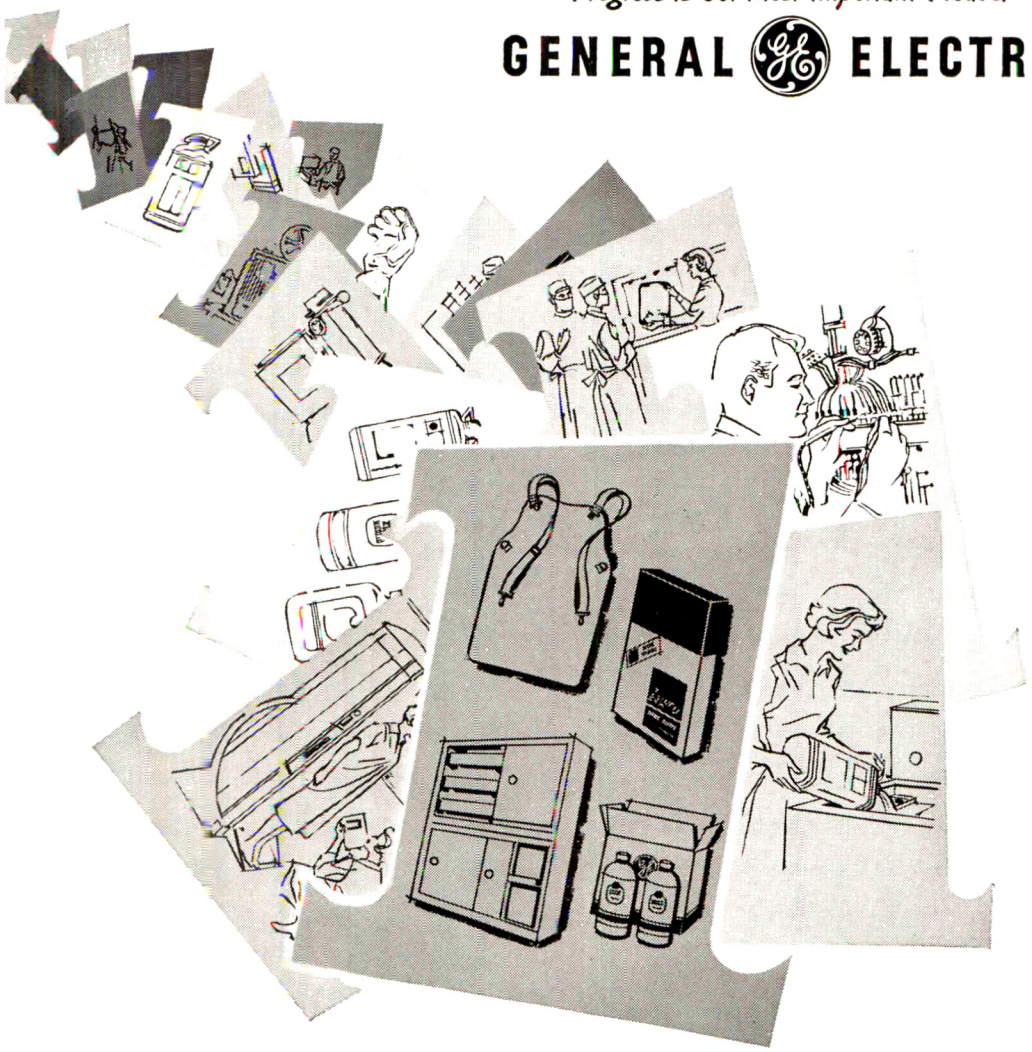


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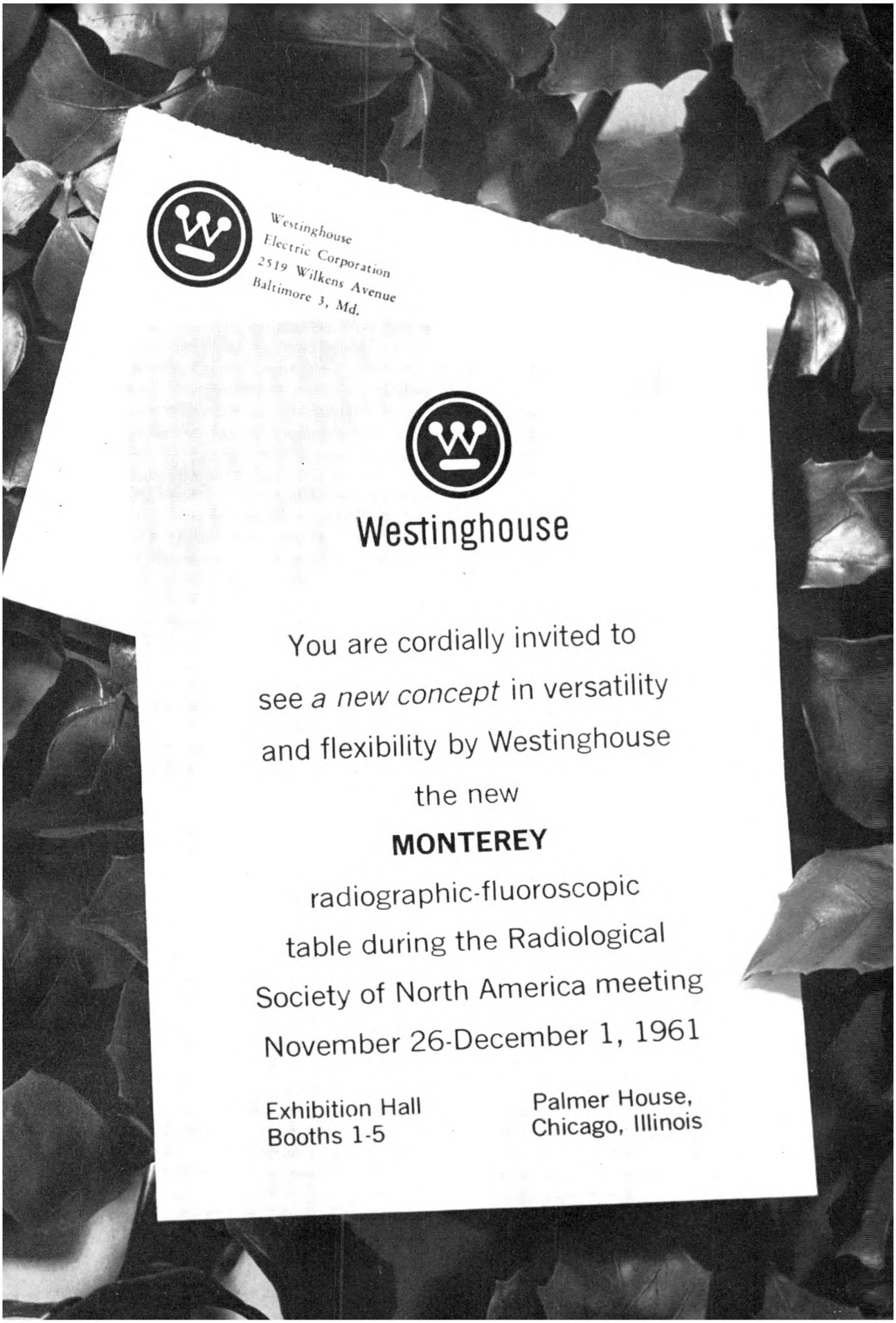
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THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 86 NOVEMBER, 1961 No. 5

CALCUTTA

INTEGRATED RADIOLOGY*

PRESIDENT'S ADDRESS

By TRAIAN LEUCUTIA, M.D.
DETROIT, MICHIGAN

IT IS with a sense of great humility that at this, the Sixty-second Annual Meeting, I assume the Presidency of the American Roentgen Ray Society. To be elected President of the oldest radiologic organization in America is a coveted distinction far beyond my desert and I should like first of all to express my profound gratitude for the honor bestowed upon me. My ardent hope is that I may prove worthy of the confidence placed in me and that I may be able to serve you conscientiously in the tradition established by a long array of illustrious predecessors and so laudably exemplified by Dr. Reineke, my immediate predecessor.

Dr. Reineke, in his scholarly dissertation of last year,[1] called attention to certain "trends and attitudes" in radiologic practice, which have developed during recent years and he admonished all of us not to sail our bark of ambition into the "trade winds" which may lead us onto the shoals of illusion and into the banks of disappointment, but rather we should steer into the quiet coves of refuge where we might meditate and consider the present and future direction of our voyage.

While Dr. Reineke spoke on the important aspect of the over-all practice of radiology and the ethics involved, of equal importance are the trends and attitudes in regard to future organizational set-ups of radiology in our country. With this view in mind I have chosen as a topic of my Inaugural Address "Integrated Radiology." I have chosen this topic for two reasons. First, the discovery of man-made radiations in 1895 by Röntgen, soon followed by the discovery of earthborn natural radiations and later by the development of artificially produced radiations, has resulted in the short span of 65 years in such amazingly rapid progress and vast expansion of the medical utilization of these radiations that, although Radiology was recognized early as a Specialty, certain trends were noted and attitudes expounded to divide this Specialty into three major disciplines, independent from each other, and more recently some consideration is being given to even further division into various subspecialties. Secondly, our Society, historically, reflects better than any other radio-

[1] REINEKE, H. G. Whither bound? President's address, 1960. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1960, *84*, 809–812.

* From the Department of Radiology, Harper Hospital, and Wayne State University, Detroit Michigan. Presented at the Sixty-second Annual Meeting of the American Roentgen Ray Society, Miami Beach, Florida, September 26–29, 1961.

logic organization the chronologic sequence of these trends and through its official JOURNAL has realistically expressed their impact on the Specialty as a whole, by scrupulously guarding at the same time the principle of Integrated Radiology.

The early workers, among which were many members of this Society, by courage, determined efforts and unrelenting perseverance overcame the many adversities particularly inherent in the medical application of such lethal agents as the roentgen rays and radium. Many successes were achieved, and to quote Sir Thurston Holland[2] "If it was at the time a bit of a nightmare . . . one has forgotten the failures, but has not forgotten the successes."

A perusal of the *American X-Ray Journal* and the *Transactions of the American Roentgen Ray Society* published in those early days reveals that almost everything in our present day practice of radiology had been conceived and to some degree elaborated before 1906. The position of roentgenology as a separate "Department of Medical Science" was clearly recognized and Dr. Hickey in 1906 wrote in the first editorial of THE AMERICAN QUARTERLY OF ROENTGENOLOGY[3]: "The roentgenologist should maintain always the position of consultant, who gives diagnostic conclusions based upon special lines of investigation. In regard to treatment, he should not allow himself to be dictated to either as to the number or character of his treatments."

After this first heroic decade progress has occurred at a swift pace. It soon became evident, however, that the tremendous accumulation of radiologic knowledge could not be stored in one single mind and that the ever-broadening scope of this knowledge in the medical field could be better achieved by devoting special attention to a branch of knowledge for which a person is distinguished. Thus the idea of a specialist within the specialty originated and since the 1920's radiology has been practiced more and more in the form of two distinct disciplines: Diagnostic Roentgenology and Therapeutic Radiology. Diagnostic Roentgenology fully emerged from its position of a "unicellular plant" in some obscure basement room and in the words of Dr. Reynolds[4] "stands at the crossroads of the corridors of the hospital forming the keypoint from which knowledge is disseminated in many directions to the benefit of the patient and to the advance of medical progress." Therapeutic Radiology, encompassing the use of the roentgen rays and the radiations of some members of the earth-born radioactive families, in particular for treatment of cancer, likewise gradually grew, after many initial difficulties, into an extremely valuable force of medical science. In our country, the two Disciplines, excepting in some of the large institutes, were never completely separated from each other, although trends toward separation were noted from time to time.

Then new trends developed within both major Disciplines. The notable progress made in all phases of medicine has brought with it a greater concentration on the study and treatment of certain individual organs and systems of the human body, resulting in the creation of various subspecialties in several Disciplines other than Radiology. This new development often made it necessary for the radiologist to apply his broad fundamental knowledge and the technical methods he already acquired to specific, more limited, fields in an endeavor to become more proficient in the diagnosis, and, at times, treatment of the disease of that organ or system. The eagerness in accomplishing this important task sometimes transcended into a trend toward complete separation from the main Discipline. Sosman,[5] as early as 1940, sounded a word of warning against such a trend. "And I may

[2] THURSTAN HOLLAND, C. X-rays in 1896. *Brit. J. Radiol.*, 1938, *11*, 1–24.

[3] HICKEY, P. M. Editorial. AM. QUART. ROENTGENOL., 1906, *1*, 1. Republished in: AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1956, *75*, 2.

[4] REYNOLDS, L. Role of radiology today, its responsibility and its import upon our life. AM. J. ROENTGENOL. & RAD. THERAPY, 1948, *60*, 443–447.

[5] SOSMAN, C. M. Specialization within roentgenology. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *44*, 645–648.

warn them for you" said Dr. Sosman "that they must at the same time maintain contact and continue their cooperation with other work in Radiology, lest they become one of those ultra-specialists who digs himself deeper and deeper into his narrow pit until he thinks the rim of his hole is the horizon of knowledge."

The concentration on the study and treatment of certain individual organs or systems has brought with it even more definite trends in the realm of Therapeutic Radiology. The early practice of the use of radium or radon as operative procedures on an empirical basis by nonradiologists has been continued in many places, even after Therapeutic Radiology has become a Discipline. The great progress made in achieving accurate dosimetry, in general, has been slowed down rather significantly through the difficulty of estimating dosages with such procedures and trying to integrate them in the over-all plan of irradiation, although endeavors to correct the situation are being made. The introduction or revival of very radical surgical procedures for the treatment of cancers of certain regions and the division into subspecialties for the performance of the procedures in these regions have created radiotherapeutic problems which could have disastrous results, unless there is the closest cooperation and understanding between members of the various Disciplines participating in the treatment.

The dramatic events of World War II have given a tremendous impetus to a third major Discipline of Radiology which now is called Nuclear Medicine. Since the start of the general distribution of radioactive isotopes of nearly all the elements by the Atomic Energy Commission in 1946, this Discipline has reached unexpected proportions. At the present time, radioactive isotopes are being employed both in the diagnostic and therapeutic fields.

In the diagnostic field these are utilized for uptake studies; dilution techniques; flow or diffusion tests, mostly in conjunction with the cardiovascular system; manifold biochemical and metabolic procedures; and various scanning procedures. Many of them form an indispensable part of the routine roentgenologic examination so that, in order to emphasize their great clinical significance, the name of Diagnostic Roentgenology has been changed to that of Diagnostic Radiology.

In the therapeutic field, for obvious reasons, the application has followed very much the pattern established on the basis of clinical experience gained with the use of earthborn natural radioactive substances, but the greatest progress has been made in the use of certain isotopes, as for example, cobalt 60, cesium 137 and iridium 192 as sources for external gamma-beam teletherapy. Moreover, due to the fact that many of the radioactive isotopes, unlike radium or radon, can also be employed in solution or with appropriate liquid vehicles, considerable expansion of the use of local tissue irradiation, especially in intracavitary and interstitial applications, has resulted. In addition, a new form of treatment, the so-called internal irradiation with radioactive isotopes, has been made possible.

Clearly, all three major Disciplines: Diagnostic Radiology, Therapeutic Radiology and Nuclear Medicine, have become important and inseparable parts of the Specialty of Radiology. Within these three major Disciplines, subspecialties may at times be necessary or advantageous. On the diagnostic side, one may enumerate the cardiovascular, neurologic, pediatric, urologic, orthopedic, gastrointestinal and other branches, especially in view of the amazing advance in the utilization of the special procedures. On the therapeutic side, one may include the regional therapeutic branches, as, for instance, the head and neck; gynecologic organs; breast; genitourinary system; lymphomas, in which chemotherapy singly or in combination with radiation therapy is still in an experimental stage; and others. Nuclear Medicine is divided and is an integral part of both the branches of Diagnostic and Therapeutic Radiology.

This principle of an Integrated Radiology, with its three major Disciplines and various subspecialties is amply reflected in the history of the official organ of our Society. After its organization in 1900, the proceedings of the Annual Meetings of the Society were published in the form of "*Transactions*." By 1906, however, following the overwhelming abundance of excitement and thrills of the first decade, leaving us a great heritage of triumph over nearly insurmountable difficulties, the Society has acquired such stature in the medical world that it was deemed appropriate to establish an official Journal. It was published first as a quarterly under the title of "The American Quarterly of Roentgenology," but its scope increased so rapidly that in 1913 it was changed to a monthly publication with the name of "The American Journal of Roentgenology."

Interest in therapy, with both roentgen rays and radium, was already considerable at this time and many articles on this subject were published in the Journal. Then in 1916 the American Radium Society was founded mainly with the purpose "to promote the scientific study of radium and other sources of ionizing radiation in relation to their physical properties and their therapeutic application." In 1922, the official Journal of our Society was also made the official Journal of the American Radium Society and in 1923 its title was changed to that of "The American Journal of Roentgenology & Radium Therapy."

One decade ago, at its Annual Meeting in Washington, D.C., in 1951, the American Roentgen Ray Society "recognizing the importance of radioisotopes and the rapidity with which they have been employed within recent years, not only in diagnostic procedures but also as therapeutic agents" decided to incorporate in the title of the Journal an additional term which "would connote the Journal's interest in atomic medicine." Since then the new title has been "The American Journal of Roentgenology, Radium Therapy & Nuclear Medicine."

Since 1956, with the celebration of its Golden Anniversary, the Journal has adopted the policy of grouping together articles pertaining to a certain subspecialty of Radiology, as mentioned above, and publishing them in a single issue. This policy enables comprehensive coverage of a chosen topic of the subspecialty but, by making use of any phase by the three major Disciplines, it broadens the horizon of our knowledge and permits us to keep pace with the enormous strides which are continuously being made in the unrelentless advancement of the Specialty of Radiology as a whole.

Thus Integrated Radiology has served us well. But Integrated Radiology carries the seeds of a future even more brilliant than its glorious past. Built, as it is, on the fundamentals of the Universe, it already embraces all aspects of the man-made radiations and the earthborn natural radiations and there is every indication that soon it will be extended to the space radiations, both man-made and spaceborn, for the immeasurable benefit of mankind.

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ARTERIOSCLEROTIC NARROWING OF RENAL ARTERIES ASSOCIATED WITH HYPERTENSION*

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OVER fifty years ago Janeway[15] showed that postoperative blood pressure persisted at a significantly high level for more than a month when the renal arteries of dogs were constricted by ligatures. In 1934, Goldblatt *et al.*,[12] by means of a clamp that they devised, constricted the renal arteries in dogs. The amount of constriction which was induced varied considerably and the extent of constriction was changed over a time interval of several weeks. Constriction of one renal artery was followed by a slight to moderate elevation of blood pressure, which then tended to return toward normal levels. Constriction of both renal arteries was followed by the production of systolic hypertension to a varying degree in all of the dogs. Since the time of that experiment, much work has been performed on the relationship of renal ischemia to malignant hypertension. Recently the relationship of arteriosclerotic narrowing of the renal arteries to hypertension has been studied.

This report is based on 1,332 aortograms which were made at the Methodist Hospital, Houston, Texas, between 1953 and 1960 and which were evaluated for renal artery narrowing.

PRESENT CONCEPT

The most plausible and widely accepted present day concept regarding the etiology of renovascular hypertension is that decrease in renal artery pulse pressure by renal artery narrowing leads to the partial conversion of pulsatile to continuous blood flow in the kidneys with anoxia of the tubular cells as a result. This leads to increase in cellular membrane permeability and the release of the large renin molecule in the tubules. This enzyme acts on a plasma substrate to form a decapeptid called hypertensin I. (This substance is not the active vasoconstrictor which produces the hypertension.) Hypertensin I is converted to hypertensin II and the latter substance is the active vasoconstrictor which has been purified and shown to be five times more active than adrenalin as a vasopressor. Hypertensin II is an octapeptid and its continuous formation produces the generalized systemic hypertension which results.

An arteriosclerotic plaque near the origin of one renal artery reduces renal arterial pulse pressure and can cause malignant hypertension. The hypertension affects the entire body, including the opposite unobstructed kidney. The involved hypotensive kidney is protected from the generalized hypertension by the arteriosclerotic plaque in its renal artery so that histologic nephrosclerotic changes do not occur in this kidney. Decreased renal blood flow, glomerular filtration and sodium and water excretion result. The urine/plasma ratio of inulin is increased. The unobstructed hypertensive kidney shows the reverse effect. Revascularization of the hypotensive kidney may remove the stimulus for the production of the hypertensive cycle. If both renal arteries are narrowed, both kidneys may be protected from the hypertension and revascularization of the kidneys will result in a marked decrease in the hypertension. The malignant nephrosclerotic

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changes will not have occurred in either kidney and a dramatic response to the surgical procedure can be expected.

AORTOGRAPHY

A translumbar aortic puncture is performed with the tip of the needle above the origin of the celiac axis. Then 10 to 25 cc. of 70 per cent urokon is injected, either manually or through an automatic injector, and the film is exposed near the end of the injection. The abdominal aorta and its many branches, including both renal arteries, are well shown and arteriosclerotic narrowing of the renal arteries, usually occurring at or near their origin in the abdominal aorta, can be demonstrated. Occasionally, diffuse arteriosclerotic disease of some of the peripheral renal arteries is evident and rarely aneurysmal dilatation of one of its branches is seen. Only 25 cc. of urokon is injected in any given day, since impaired renal function and even death can result from excessive amounts of contrast material.

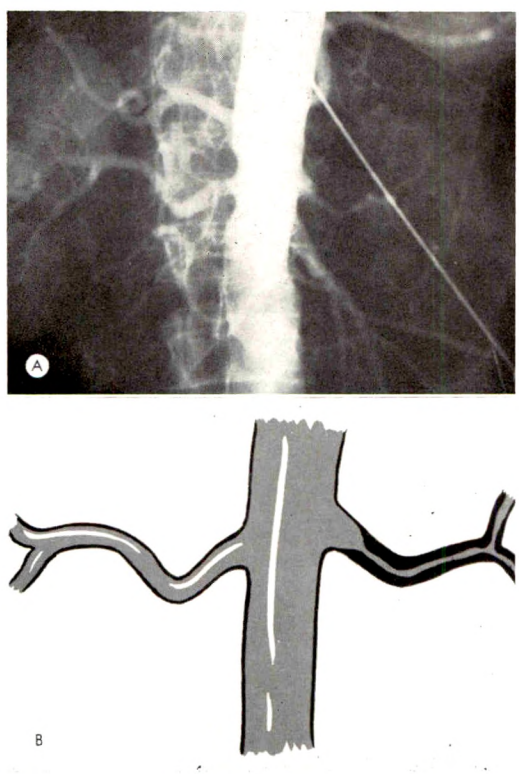


Fig. 1. Case I. (*A*) Aortogram showing diffuse narrowing of the left renal artery. The right renal artery is not significantly narrowed. (*B*) Drawing illustrating left renal artery narrowing.

ILLUSTRATIVE CASES

Case I. B.S., a white male, seventy-six years old, had had moderate hypertension for twenty years and a known abdominal aortic aneurysm at the time of admission. Aortography demonstrated diffuse narrowing of the left renal artery (Fig. 1, *A* and *B*). An excretory pyelogram revealed impaired function of the left kidney. The abdominal aortic aneurysm was resected and replaced with a graft. Although, the left kidney was noted at surgery to be atrophic, no operative procedure was performed on it or on the left renal artery. The patient has remained well since the operation but the moderate hypertension has persisted.

Case II. F.S., a white male, sixty-eight years old, had an eight months' history of frontal and occipital headaches and hypertension. Renogram showed vascular insufficiency on the left. The aortogram (Fig. 2, *A* and *B*) disclosed stenosis of the left renal artery just proximal to its bifurcation with poststenotic dilatation. Endarterectomy with patch grafting was performed on the left renal artery and a postoperative aortogram (Fig. 2, *C* and *D*) showed successful removal of the arteriosclerotic plaque in the left renal artery. The patient's postoperative blood pressure was normotensive.

Case III. J.M., a white male, fifty-two years old, had a one year history of hypertension and headaches. He presented with an enlarged heart and generalized arteriosclerosis. The aortogram (Fig. 3, *A* and *B*) demonstrated right renal artery stenosis and an abdominal aortic aneurysm. The aneurysm was resected and a graft extending from the abdominal aorta to both common iliac arteries with a limb up to the right renal artery was inserted (Fig. 3, *C*, *D* and *E*). The patient was normotensive postoperatively.

Case IV. E.M., a white female, forty-nine years old, gave a history of progressive hypertension of two years' duration with headaches, scotomata and syncopal episodes. The blood pressure ranged from 190/90 to 240/125 mm. of mercury. Split renal function studies showed a slight reduction of sodium and water excretion and of inulin and para-aminohippuric acid

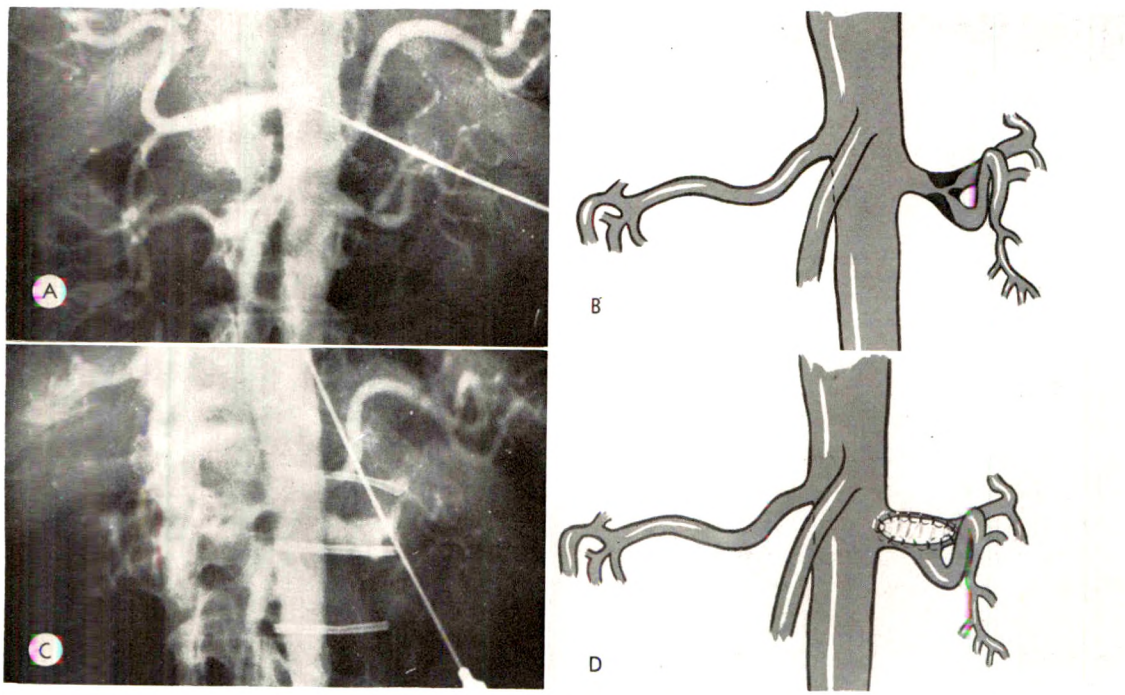


Fig. 2. Case II. (*A*) Aortogram demonstrating narrowing of the left renal artery; note also the early bifurcation. (*B*) Drawing illustrating the renal artery narrowing. (*C*) Postoperative aortogram showing the results of endarterectomy and patch grafting. (*D*) Drawing of the patch graft.

clearance in the right kidney. The aortogram (Fig. 4, *A* and *B*) revealed stenosis of the right renal artery. A bypass graft was inserted which extended from the abdominal aorta to the right renal artery (Fig. 4*C*). Postoperatively, the patient's blood pressure was in the normotensive range.

Case V. L.S., a white female, forty-eight years old, had a blood pressure of 180/90 to 220/120 mm. of mercury; her hypertension was first discovered six weeks before hospitalization. The aortogram (Fig. 5) demonstrated lower pole accessory renal arteries bilaterally with slight narrowing and poststenotic dilatation in the accessory right renal artery. There was a pulse pressure gradient in the accessory right renal artery. The patient underwent patch graft angioplasty to the accessory right renal artery and after operation she was normotensive.

Case VI. H.R., a white male, fifty-seven years old, had moderate hypertension of three years' duration with increasing claudication in both legs during that period. The aortogram (Fig. 6) demonstrated complete occlusion of the abdominal aorta just below the level of the renal arteries. Aortic-femoral bypass grafts were inserted and the patient had complete relief of the claudication; however, the moderate hypertension persisted. An occluded lower pole accessory right renal artery was suspected from the aortographic findings.

Case VII. A.N., a white male, forty-three years old, had symptoms of malignant hypertension of two months' duration. The blood pressure ranged from 190/100 to 280/150 mm. of mercury. Hypertensive retinopathy had produced almost complete blindness. An excretory pyelogram revealed delayed excretion by the right kidney. An aortogram (Fig. 7*A*) demonstrated stenosis of the right renal artery. An aortic-iliac bypass procedure was performed with a limb extending up to the right renal artery (Fig. 7*B*). Postoperatively, the patient was normotensive; the hypertensive retinopathy subsided and vision was normal within three weeks.

Case VIII. W.D., a white male, fifty-nine years old, was referred because of an abdominal aneurysm. The patient had moderately severe hypertension. An aortogram (Fig. 8*A*) revealed stenosis of the proximal portions of each renal artery. The abdominal aortic aneurysm was

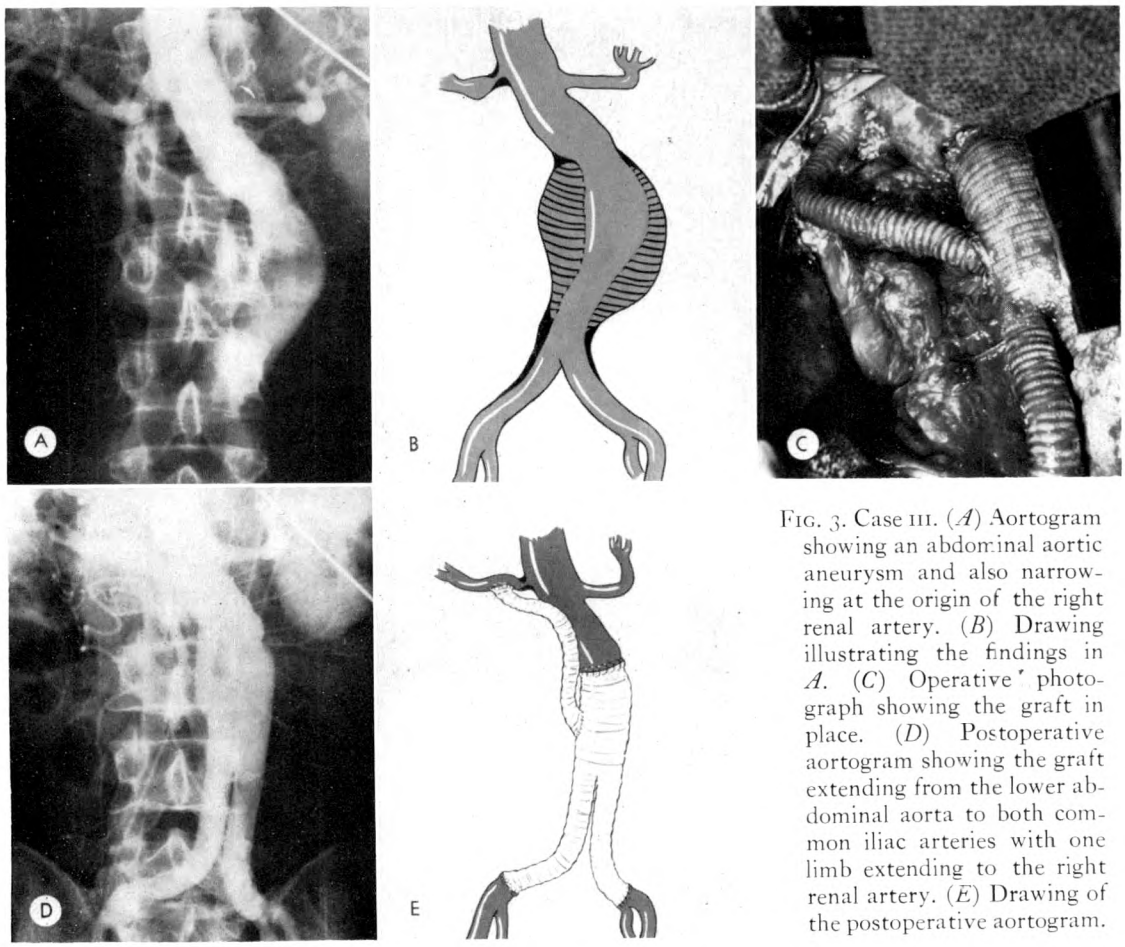


Fig. 3. Case III. (*A*) Aortogram showing an abdominal aortic aneurysm and also narrowing at the origin of the right renal artery. (*B*) Drawing illustrating the findings in *A*. (*C*) Operative photograph showing the graft in place. (*D*) Postoperative aortogram showing the graft extending from the lower abdominal aorta to both common iliac arteries with one limb extending to the right renal artery. (*E*) Drawing of the postoperative aortogram.

resected and replaced by a dacron graft and limbs from the graft were extended to each renal artery (Fig. 8*B*). Postoperatively, the patient had moderate reduction of the hypertension.

Case IX. L.H., a white male, fifty years old, had had resection and homograft replacement of the aortic bifurcation in 1953 for occlusive disease. Following this, the patient had increasing hypertension for two years. The blood pressure range was 200/90 to 240/130 mm. of mercury. An aortogram (Fig. 9*A*) revealed narrowing of the left renal artery and a graft was inserted extending from the abdominal aorta homograft to the left renal artery (Fig. 9*B*). Postoperatively, the patient had a blood pressure range of 118/80 to 160/85 mm. of mercury.

Case X. C.T., a white female, fifty-five years old, had hypertension of six years' duration with repeated black-out spells, numbness of the left arm and claudication of the left leg. After a right carotid endarterectomy was performed, an aortogram (Fig. 10) revealed narrowing of the right renal artery and of the lower pole accessory left renal artery. Resection and graft replacement of the aortic bifurcation with a patch graft angioplasty of the right renal artery were done. The patient has remained asymptomatic since the operation, although mild hypertension has persisted. The latter is probably explained on the basis of the narrowed accessory left renal artery.

Case XI. J.H., a white female, fifty-seven years old, had hypertension of five years' duration with progressive claudication for three years. The blood pressure range was 160/90 to 220/120 mm. of mercury. An aortogram (Fig. 11*A*) revealed narrowing of the left renal artery at its origin and an excretory pyelogram (Fig. 11*B*) showed impaired function of the left kidney. An aortic-femoral bypass graft was in-

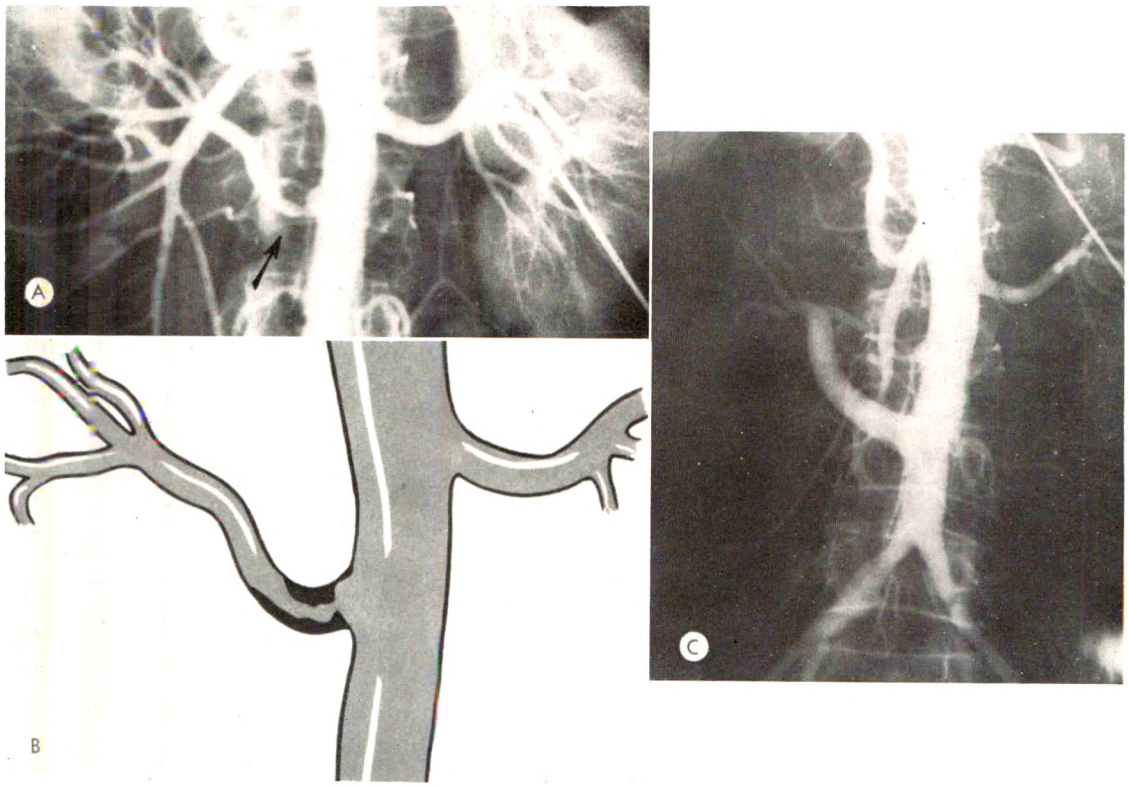


Fig. 4. Case iv. (*A*) Aortogram showing narrowing of the right renal artery (arrow). (*B*) Drawing illustrating narrowing of the right renal artery. (*C*) Postoperative aortogram showing the limb of the graft extending to the right renal artery.

serted bilaterally with a limb extending up to the left renal artery. The blood pressure postoperatively remained within the normotensive range and there was no longer any claudication.

Case xii. H.G., a white male, sixty-four years old, had hypertension and a history of right hemiplegia with subsequent recovery. An aortogram (Fig. 12) revealed moderate narrowing of the left renal artery at its origin. A left renal artery bypass graft was inserted as well as aortic-iliac grafts and the patient was normotensive postoperatively.

Case xiii. H.W., a white male, fifty-five years old, had hypertension of several years' duration with progressive claudication of both legs for two years. The blood pressure range was 210/110 to 260/120 mm. of mercury. The

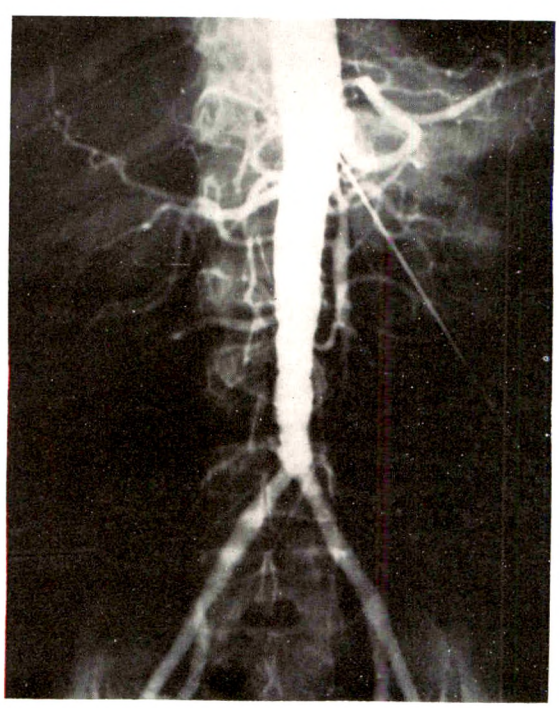


Fig. 5. Case v. Aortogram showing lower pole accessory renal arteries bilaterally. There is slight narrowing with poststenotic dilatation on the right.

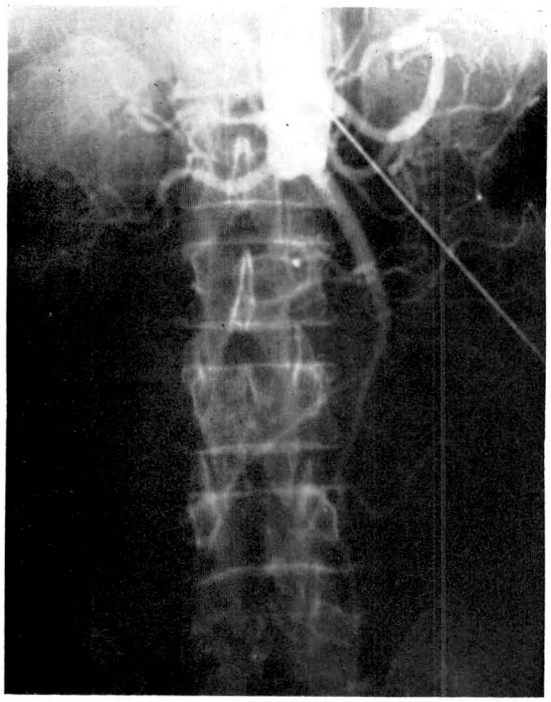


FIG. 6. Case VI. Aortogram illustrating the usual location for complete abdominal aortic occlusion. An occluded anomalous renal artery to the lower pole of the right kidney was suspected.

renogram revealed decreased vascularity of the left kidney and an aortogram (Fig. 13) showed stenosis of the left renal artery. A bilateral aortic-femoral bypass graft with a limb extending up to the left renal artery was inserted and the patient's blood pressure gradually declined to 140/80–160/90 mm. of mercury.

CASE XIV. W.B., a white male, forty-nine years old, had a three year history of hypertension and dizziness. An aortogram (Fig. 14) revealed stenosis of the right renal artery. An aortic-femoral right renal bypass graft was inserted and the patient was normotensive postoperatively.

CASE XV. R.S., a white male, forty-nine years old, had claudication in the right leg for two years with no history of hypertension. The aortogram (Fig. 15) revealed bilateral accessory renal arteries with slight narrowing at the origin of the right lower renal artery. The patient underwent endarterectomy of the right common iliac artery with complete relief of the claudication. His blood pressure remained normal.

RESULTS

A three-man team reviewed 1,332 lumbar aortograms and evaluated the appearance of the renal arteries. Most of the patients

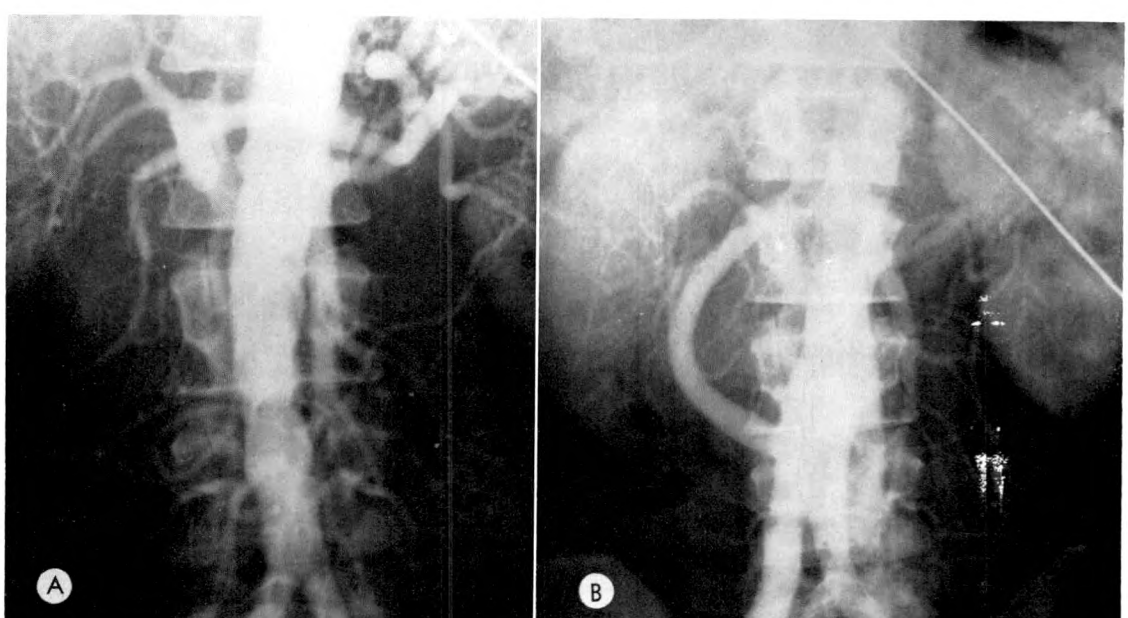


FIG. 7. Case VII. (*A*) Aortogram illustrating almost complete occlusion of the right renal artery. (*B*) Postoperative aortogram showing the limb of the graft extending to the right renal artery.

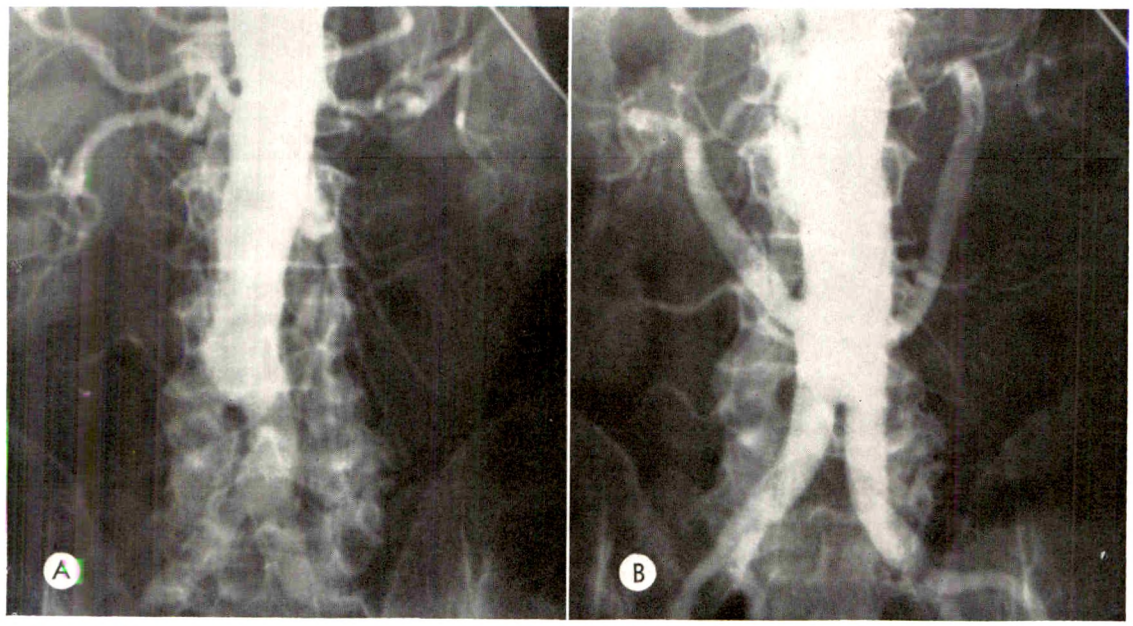


Fig. 8. Case viii. (*A*) Aortogram demonstrating narrowing of both proximal renal arteries. (*B*) Postoperative aortogram showing a limb of the graft extending to each renal artery.

had aortography performed because of aneurysm or occlusive disease in the abdominal aorta or because of circulatory impairment to the lower extremities. In other words, most of these cases had advanced arteriosclerotic disease as the cause of their presenting complaint and relatively few of the examinations were done primarily for the evaluation of hypertension. Renal artery anomalies were noted and kidney size and renal function were estimated by means of a follow-up pyelograms which, in most cases, had been taken ten minutes following the aortogram. Arteriosclerotic disease of the abdominal aorta and other branches was also noted. (This was found to be present in a very high percentage of the cases.) The age

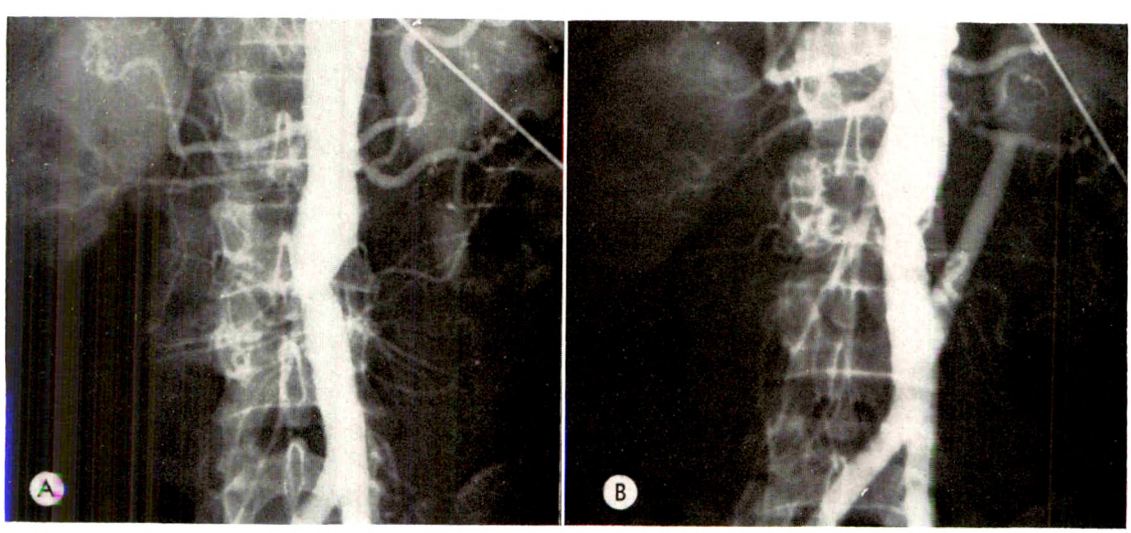


Fig. 9. Case ix. (*A*) Aortogram demonstrating stenosis of the left renal artery. (*B*) Postoperative aortogram showing the graft to the left renal artery.

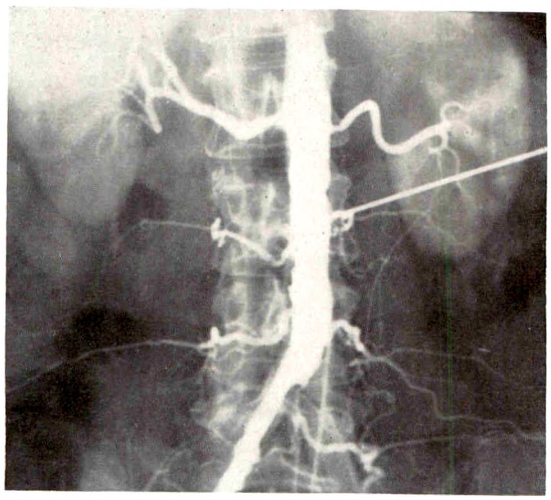


FIG. 10. Case x. Aortogram made after a low aortic injection and showing stenosis of the right and inferior accessory left renal arteries. (This type of needle placement has been discarded because it can cause intramural dissection in a diseased aorta and renal artery occlusion may follow.)

range of the patients was eighteen to eighty-six years. The average age was fifty-five years.

Of the 1,332 aortograms, 437 were judged technically unsatisfactory for this study, since the renal arteries were not adequately visualized. Motion of the patient, improper centering of the film, excess dilution of contrast material, extravasation of contrast material, superimposition of other arteries over the renal vessels and direct injection into the celiac axis or superior mesenteric artery were some of the causes for inadequate demonstration of the renal arteries; however, most of these 437 studies were unsatisfactory because the aortic puncture was below the level of the renal arteries. (Injection at this level is discouraged at the present time because of the possibility of producing a dissecting aneurysm at the site of the needle puncture, since arteriosclerotic changes are usually more severe in the lower abdominal aorta than in the upper.) Also, the aortograms of 74 patients who had no blood pressure readings recorded on their hospital charts were not considered. This left a total of 821 aortograms which were used in the present series

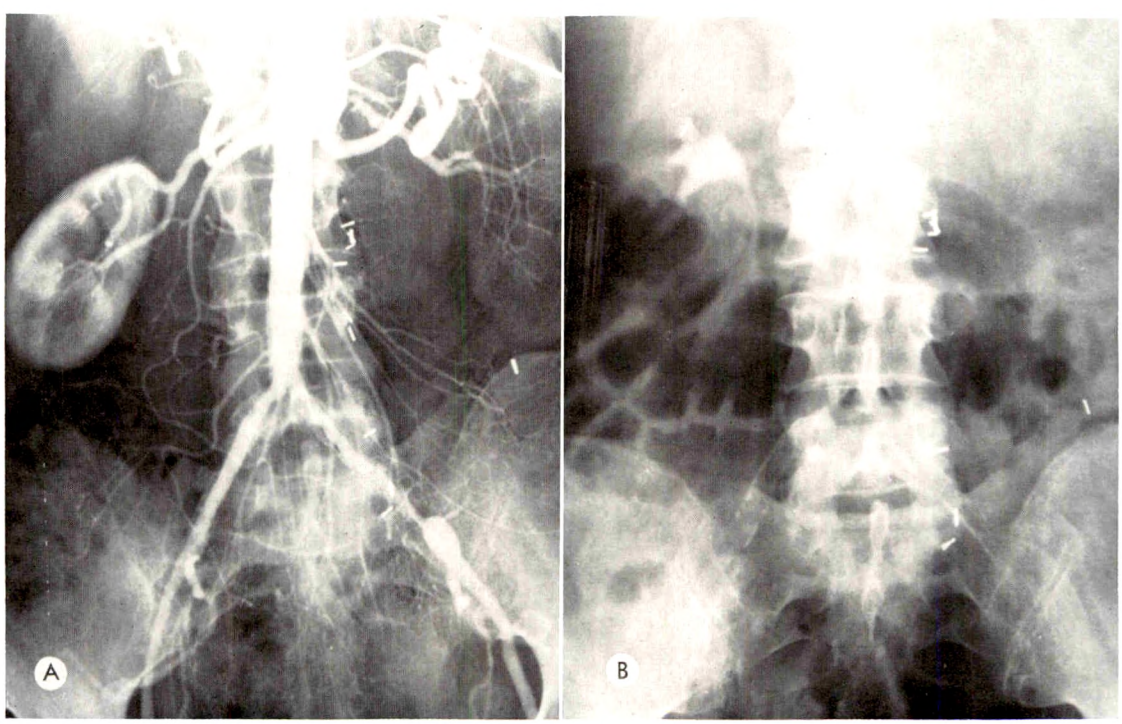


FIG. 11. Case xi. (*A*) Aortogram showing stenosis of the left renal artery. (*B*) Follow-up excretory pyelogram revealing impaired function of the left kidney.

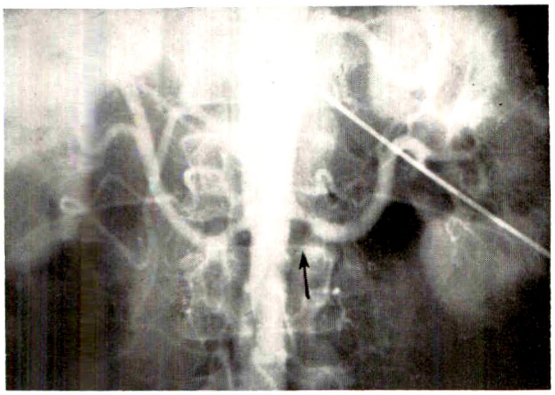


Fig. 12 Case xii. Aortogram demonstrating stenosis of the left renal artery (arrow).

for the statistical evaluation of arteriosclerotic disease of the renal arteries and its relationship to hypertension (Table I).

The criteria for hypertension are, of course, a very important aspect of this statistical analysis and a slight change in the criteria will make a significant difference in the statistics.

The blood pressure readings were taken from the hospital charts and usually totaled six recordings. The first two, the last two, and the highest two readings were tabulated. Table II shows the results when, as criteria for hypertension, two of the six blood pressure recordings showed a systolic or diastolic hypertension, or when there was one systolic and one diastolic elevation. These criteria were purely arbitrary and do not constitute a very strict definition.

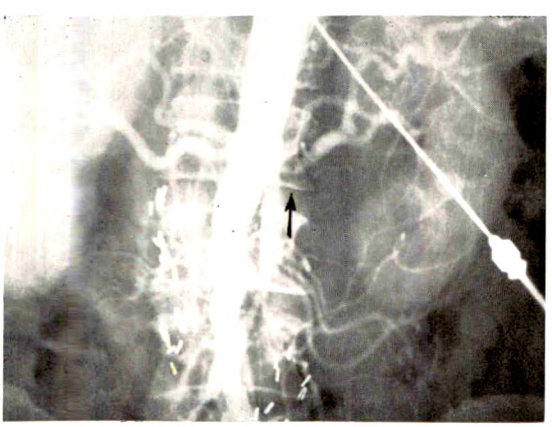


Fig. 13. Case xiii. Aortogram demonstrating stenosis of the left renal artery (arrow).

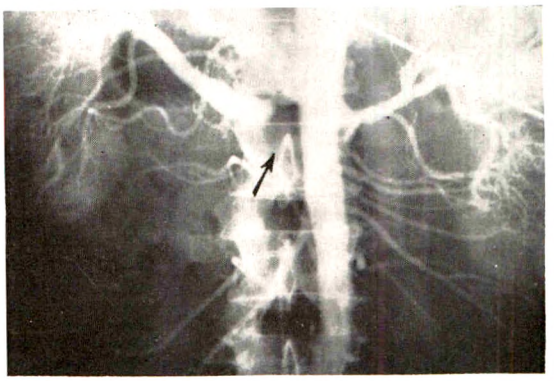


Fig. 14. Case xiv. Aortogram demonstrating stenosis of the right renal artery (arrow).

Many of the patients, however, were on medication for the treatment of hypertension. On the other hand, of course, errors can be made in the taking of the blood pressure.

Any diastolic recording over 90 mm. of mercury was considered hypertensive at any age. The baseline for the systolic hypertensive level was taken from insurance

Table I

Material

Total aortograms reviewed	1,332
Aortograms with inadequate visualization of renal arteries	437
Cases with no blood pressure readings recorded	74
Aortograms and cases used	821

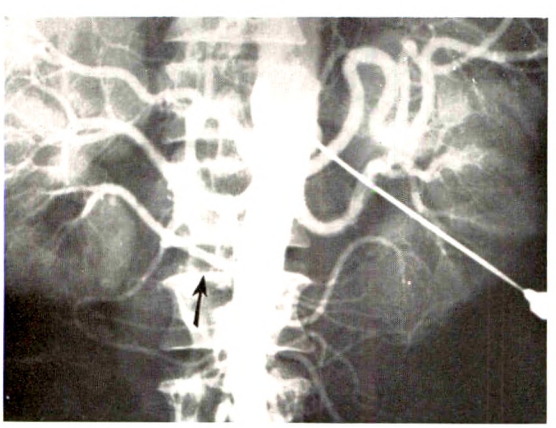


Fig. 15. Case xv. Aortogram demonstrating bilateral accessory renal arteries with stenosis evident on the right (arrow).

Table II

RENAL ARTERY STENOSIS AND HYPERTENSION*

(821 cases)

	No. of Cases	Per Cent
Hypertension	643	78.3
No hypertension	178	21.7
Renal artery stenosis (unilateral or bilateral)	416	50.7
Hypertension and renal artery stenosis	358	43.7
Arteriosclerotic occlusive disease (aortic, iliac, femoral or popliteal arteries)	737	89.7

* Criterion for hypertension; two of the six blood pressure readings showing a systolic or diastolic elevation; or one systolic and one diastolic elevation.

company statistical analyses of normal levels of blood pressure in various age groups. Under forty years of age, 140 mm. of mercury was considered the dividing line between normotension and hypertension. For each succeeding decade after forty, 5 mm. of mercury is added to give the upper limits of normotension in the population of the United States as a whole.

Table II shows that 78.3 per cent of the total 821 patients had hypertension; 50.7 per cent had narrowing of one or both renal arteries demonstrated by aortography, and 43.7 per cent had both hypertension and renal artery narrowing. Unilateral narrowing was slightly more common than bilateral and the right artery was stenosed slightly more frequently than the left (Table III). Associated arteriosclerotic disease (in the abdominal aorta, iliac, femoral or popliteal arteries) was present in almost all the cases (89.7 per cent).

A ten minute excretory pyelogram was usually made following the aortogram and this was evaluated for evidence of impaired renal function. Many authors describe absent or delayed excretion of contrast material as a sign of impaired blood supply to a kidney and some consider that a definitely smaller kidney on one side indicates impaired renal function. These signs, when present, were usually found to be in the patient who had aortographic evidence of narrowing of a renal artery. However, in the overwhelming majority of the cases, excretion of contrast material and kidney size were normal (Table IV). It appeared to us that excretory pyelography following aortography adds very little to the evaluation of the blood supply to the kidneys.

Each renal artery in the 821 aortograms was judged as normal, questionably diseased, showing definite evidence of arteriosclerosis, or inadequately visualized for technical reasons.

The accessory renal arteries were not tabulated but it was our general impression that they are frequently present, and

Table III

RENAL ARTERY STENOSIS AND HYPERTENSION*

(821 cases)

	No. of Cases			Per Cent
Renal artery stenosis (unilateral or bilateral)	416			50.7
Hypertension		358		43.7
Bilateral renal artery stenosis			155	18.9
Unilateral renal artery stenosis			203	24.8
Right renal artery stenosis			107	13.1
Left renal artery stenosis			96	11.7
No hypertension		58		7.0
Normal renal arteries, bilaterally	235			28.7
Hypertension		154		18.8
No hypertension		81		9.9

* Same criterion for hypertension as in Table II.

TABLE IV

RENAL ARTERY STENOSIS AND HYPERTENSION*
(821 cases)

	No. of Cases	Per Cent
Associated arteriosclerotic disease (aorta, iliac, femoral or popliteal arteries)	737	89.7
Nonvisualization of a kidney on the pyelogram	2	0.2
With hypertension and renal artery stenosis	1	0.1
Contracted kidney	8	1.0
With hypertension and renal artery stenosis	6	0.7
Delayed excretion	62	7.5
With hypertension and renal artery stenosis	46	5.6

* Same criterion for hypertension as in Table II.

as many as three renal arteries to a kidney were seen. A low accessory renal artery frequently is partially or completely occluded and many times an occluded renal artery not visualized on the aortogram can be suspected because of a relatively avascular area (usually the lower pole) seen on the nephrogram.

When the criteria for hypertension were varied slightly there was a significant effect on the statistics. A second statistical analysis of the association of arteriosclerotic narrowing and hypertension was made when, as the criterion for hypertension, three of the six systolic or two of the six diastolic recordings were over the limit for the age of the patient (Table V). Of the total 821 cases, 54.5 per cent had hypertension and 33.7 per cent had both hypertension and renal artery stenosis.

CONCLUSIONS

Of the total 821 cases, 43.7 per cent had both renal artery narrowing and hypertension (Table II). Arteriosclerotic disease of other arteries was almost always present. Delayed or absent excretion of contrast material by a kidney or the presence of a contracted kidney was not evident with any significant frequency. When more stringent

TABLE V

RENAL ARTERY STENOSIS AND HYPERTENSION*
(821 cases)

	No. of Cases	Per Cent
Hypertension	447	54.5
No hypertension	374	45.5
Renal artery stenosis	417	50.7
Hypertension and renal artery stenosis	276	33.7

* Criterion for hypertension: three of the six blood pressure readings showing a systolic elevation; or two diastolic elevations.

hypertension criteria were utilized, 33.7 per cent of the 821 cases had both hypertension and renal artery disease (Table V).

SUMMARY

In a review of 1,332 aortograms, 821 were found satisfactory for evaluation of the renal arteries. The hospital charts of the 821 cases were studied and blood pressure readings were recorded. The statistical relationship of renal artery narrowing to hypertension was tabulated.

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ANALYSIS OF THE RADIO-RENOGRAM CURVE*

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THE use of the I^{131} renogram as a test for kidney function has been described.[4,6] The chief application of this procedure is as a screening test to rule out unilateral renal disease in hypertensive persons,[5] and to detect gross abnormalities in renal function that involve large portions of kidney parenchyma.[1] The major limitation in its use is that this test is essentially qualitative and subject to individual interpretation.[2]

The work presented here proposes a method of analysis of the radio-renogram that permits a more objective interpretation.

METHOD

Patients are placed on a bed in a prone position. The anatomic location of the kidneys is determined beforehand by abdominal roentgenography. A 2 inch sodium iodide (Tl) scintillation crystal in a lead collimated probe is placed over each kidney. A third scintillation detector is placed over the posterior thorax at the level of the heart. Each detector is connected to a count rate meter and then to a rectilinear strip chart recorder.

One microcurie of I^{131} labeled hippuric acid per 3 kg. of body weight is injected intravenously. The levels of radioactivity over each kidney and the heart are recorded.

Control renograms were made of 50 healthy university students. Renograms were also made of 22 hospital patients with hypertension. One or more of the standard renal function tests, including intravenous pyelography, phenolsulfonphthalein excretion, aortography, differential clearance studies, and blood and urine chemistries were also performed. On the basis of these clinical tests, these patients were found to have no renal dysfunction associated with their hypertension. In addition, renograms were made of a group of 9 patients with clinically proved renal disease.

RESULTS

A normal hippuric acid renogram is shown in Figure 1. Characteristically, it has the three segments described by Taplin *et al.*[3] The first, or vascular, segment is shown by the portion of the curve labeled *AB*. The second, or concentration, phase is *BC*. The third, or excretory, segment is shown by *CEF*; *F* being the point at which a new base line or equilibrium is reached.

In order to make the analysis for this study, each renogram was prepared as follows: from point *B* a horizontal line was drawn to intersect *CF* at point *E*. Vertical lines were then drawn from points *B*, *C*, and *E* to the base line. The time elapsed during the vascular segment of the curve is represented by t_b; the duration of the concentration segment is t_c; and t_e is the time during which the curve returns to a value equal to the height of the vascular peak.

To achieve standardization of the renograms the following considerations were made.*

1. "*X*" is equal to the maximum blood level of I^{131}.
2. "*Y*" is the peak of the concentration phase of the renogram curve.
3. Then $100(Y-X)/X$ is the percentage of the maximum blood level concen-

* For the purposes of this study and the development of arbitrary expressions of kidney function, the mathematic assumptions made are adequate. The authors acknowledge the fact that an accurate quantitative analysis of the renogram curve would involve considerations more complex than the linear relationships expressed herein.

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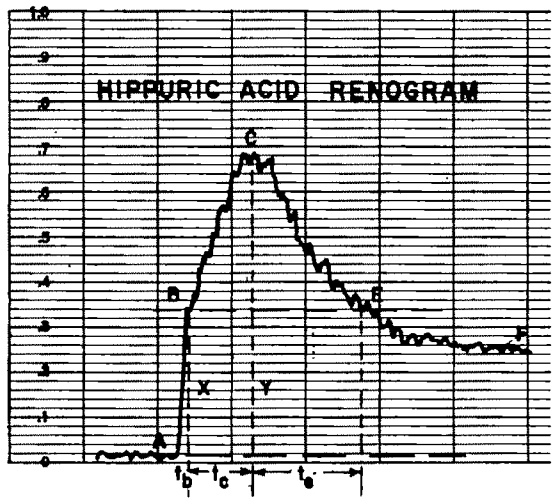


FIG. 1

trated by the kidney, or total concentration.

4. Total concentration divided by time t_c equals the percentage concentrated per minute, or minute concentration.
5. Total concentration divided by time t_e equals the percentage excreted per minute, or minute excretion.

The renograms are divided into three groups. Group I is the control group. Group II consists of the hypertensive patients with no demonstrated kidney disease. Group III is composed of those patients with unilaterally or bilaterally abnormal kidney function (demonstrated by tests other than the renogram).

The total concentration, minute concentration, and minute excretion values were determined for the left and right renogram curves of each person tested. The mean values and standard deviations of these determinations for the renograms in Groups I and II are shown in Table I and II.

Table III lists the results of the renograms made of the patients in Group III; that is, those with abnormal kidney function.

DISCUSSION

From the data in Table I it can be seen that, in the control group, there is no significant statistical difference in the normal values between the left and right renogram curves.

Similarly, a comparison of the renograms in the second group also shows no statistical difference between the values for the left and right renogram curves.†

In comparing the total concentration and minute concentration of Groups I and II with each other, it is seen that, as a whole, the hypertensive group has significantly lower levels ($p < .01$) of these two parameters than the control group. This disparity is more evident when comparisons between the minute excretion values of these two groups are made ($p < .005$). When considered individually, however, the majority of the hypertensive patients fall within the normal limits as defined by the control

† This study was originally undertaken using I^{131} diodrast as the test agent, and a wide divergency of normal values was found between the left and right renograms, presumably due to the concentration of diodrast in the liver. For this reason we have abandoned this compound in favor of I^{131} hippuric acid.

TABLE I

GROUP I—NORMAL CONTROLS

	Total Concentration (per cent)		Minute Concentration (per cent)		Minute Excretion (per cent)	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Left Kidney	72.1	27.1	20.6	8.9	17.4	9.1
Right Kidney	73.7	31.8	20.0	9.8	16.9	9.0
Average of Both Kidneys	72.9	29.5	20.3	9.3	17.1	9.0

Table II

GROUP II—HYPERTENSIVE PATIENTS WITH NORMAL KIDNEY FUNCTION

	Total Concentration (per cent)		Minute Concentration (per cent)		Minute Excretion (per cent)	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Left Kidney	54.9	26.8	17.7	7.2	11.0	7.1
Right Kidney	55.1	28.6	15.7	6.2	10.3	4.6
Average of Both Kidneys	55.0	27.7	16.7	6.7	10.6	5.8

group. As the number of normal and hypertensive patients in this study is increased, it may be possible to evaluate more fully the significance of this difference between the two groups.

Table III shows that the value of one or more of the three renogram parameters for the patients in the third group falls outside the normal limits given by the control group.

Table III

GROUP III—PATIENTS WITH ABNORMAL KIDNEY FUNCTION

Patient	Kidney	Total Concentration (per cent)	Minute Concentration (per cent)	Minute Excretion (per cent)	Clinical Diagnosis
1	Left	60.0	18.9	3.6	Chronic glomerulonephritis
	Right	27.5	8.7	2.4	
2	Left	53.1	18.1	4.9	Chronic glomerulonephritis
	Right	80.2	26.0	5.9	
3	Left	88.0	2.7	0.0	Left hydronephrosis;
	Right	22.0	2.7	1.4	Nonfunction of right kidney
4	Left	314.0	18.8	0.0	Acute glomerulonephritis
	Right	104.0	9.0	0.0	
5	Left	148.0	11.3	5.5	Chronic glomerulonephritis
	Right	178.0	17.5	7.4	
6	Left	167.5	4.9	0.0	Left hydronephrosis;
	Right	0.0	0.0	0.0	Nonfunction of right kidney
7	Left	14.9	8.1	9.4	Chronic pyelonephritis
	Right	23.8	10.6	6.8	
8	Left	168.0	9.6	0.9	Left hydronephrosis;
	Right	102.0	22.8	9.6	Normal right kidney
9	Left	106.0	5.5	0.0	Bilateral hydronephrosis
	Right	16.7	1.1	0.0	

CONCLUSION

A method for analysis of the radio-renogram is proposed. This method eliminates certain variables inherent in this procedure and permits a more objective interpretation of the renogram curve.

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EXTRARENAL CALYCES: THEIR RELATIONSHIP TO RENAL DISEASE*

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A RARE congenital anomaly of the renal pelvis and calyces, which has evoked little interest in the past, has been encountered with increasing frequency due to the awareness and recognition of this abnormality. Although it may appear as an incidental finding at postmortem examination, more often it has been found associated with renal disease. Reports describing extrarenal calyces have been sparse in the urologic literature, and our series of 8 cases suggests that this anomaly may occur more commonly than the literature would indicate.

CASES REPORTED IN THE LITERATURE

Eisendrath[2] presented a case of calculous hydronephrosis with extrarenal calyces and discussed 3 previously reported cases. The first of these, described by Fürstner, was a case in which the extrarenal calyces were present in a hypoplastic segment of a bifid kidney. The second case, mentioned by Herz, was one of bilateral extrarenal calyces. In the third case, reviewed by Apert, the extrarenal calyces entered the ureter without an intermediate pelvis. A case similar to that of Eisendrath was reported by Veseen.[3] In 1951, a sixth case, described by Dunn and Gibson,[1] showed ectopia and hydronephrosis associated with this congenital anomaly.

ANATOMY

The anatomic feature (Fig. 1) of this congenital anomaly is a discoid shaped kidney, flattened in the anteroposterior diameter, with the pelvis and the major and minor calyces located outside the renal parenchyma. The hilus is elliptical and

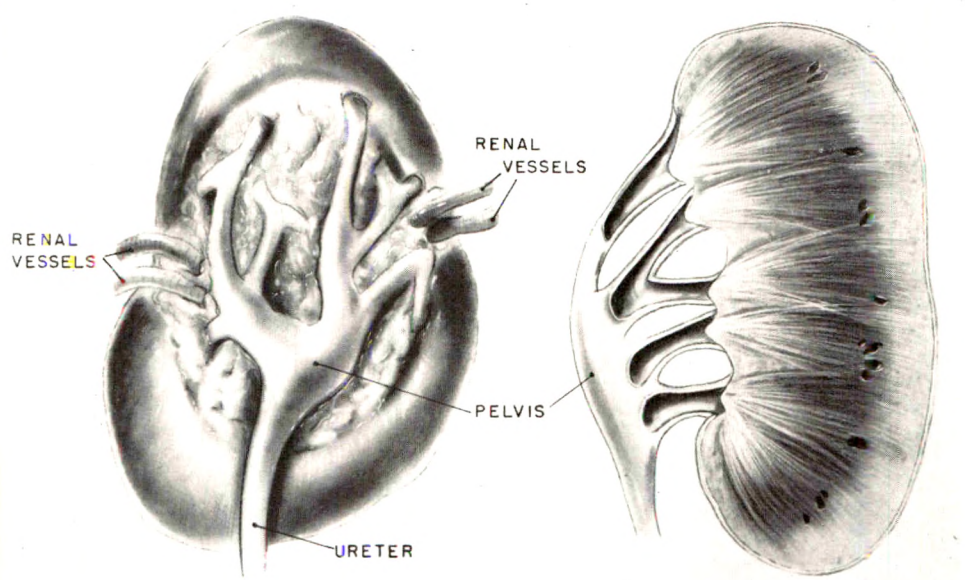


FIG. 1. Posterior aspect (left) and cross section (right) of an extrarenal calyceal system.

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covers most of the posterior surface, with the minor calyces attaching themselves to the kidney in this area. The cut section of the kidney reveals the usual appearance of cortical and medullary zones, with the papillae protruding into the minor calyceal cups, which are attached at the hilar surface. The renal vessels enter the kidney with an anomalous distribution, usually at the circumferential edge of the flat, widened hilus.

EMBRYOLOGY

The anomaly may be due to a disparity resulting from slow development of the nephrogenic anlage, or to a rapid development of the ureteric bud. At the end of the third or the beginning of the fourth week of gestation, the metanephros arises from the nephrogenic anlage and replaces the mesonephros in function. Simultaneously, the ureteric bud ascends in a cephalad direction toward the nephrogenic mass, which forms a cap around the blind end. As the growth continues, the blind end widens and invaginates, forming a cephalad and a caudad limb, representing the major calyces. Two more buds, a dorsal and a ventral, grow out of each limb, forming the four buds which constitute the major calyces; they are referred to as the collecting tubules of the first order. Each of these, in turn, produces two to four buds which develop into the minor calyces, or the collecting tubules of the second order. Should exaggerated or precocious development occur at this stage, the calyceal system could well develop prior to its coalescence with the nephrogenic mass. Conversely, a lag in the growth of the nephrogenic mass could delay its attachment to the collecting system, permitting extrarenal development of the first or second order of the collecting system.

DIAGNOSIS

This condition may be detected by excretory urography and retrograde pyelography when the renal pelvis is visualized outside the renal shadow. More characteristic is the pattern of the major calyces, which seem to flare out with a terminal incurvation, simulating the curved prongs of a small hand garden rake. When surgery is indicated, meticulous dissection of the renal hilus readily reveals the pelvis to be located in the perirenal tissues. The calyces can then be traced to their insertion in the renal parenchyma.

REPORT OF CASES

CASE I. A.C. This sixty-seven year old white male, because of continued urinary difficulties following a transurethral resection in 1946 at another hospital, had a second operative procedure in 1950 at the same hospital. The pathologic diagnosis of the tissue obtained at the second resection was adenocarcinoma of the prostate gland. Intravenous urography revealed a normal left kidney and an ectopic right kidney. On admission to the Veterans Administration Hospital in 1956 because of urinary symptoms, examination demonstrated a nonfunctioning right kidney and a normal left kidney, as well as generalized metastases. The patient expired in November, 1957. At autopsy, a typical extrarenal calyceal system of the right kidney was found. This anomaly had not caused any clinical symptoms.

CASE II. J.M. This sixty-two year old white male was admitted to the Flower Fifth Avenue Hospital in 1948 complaining of gross hematuria for the past eighteen years. This occurred at approximately six month intervals and would clear within twenty-four hours. Occasional dysuria was admitted, but no other symptoms were present. Physical examination and laboratory findings were essentially normal. The intravenous urogram and retrograde pyelogram revealed a left calculous hydronephrosis. The right side appeared normal. A left nephrectomy was performed and examination of the specimen (Fig. 2) showed extrarenal calyces attached to a discoid shaped kidney. The pelvis contained a large calculus causing urinary obstruction. The kidney exhibited advanced obstructive degeneration.

CASE III. R.B. This sixty year old white male was admitted to the medical service of the Veterans Administration Hospital suffering with diabetes, hypertension and amaurosis. Early signs of cardiac decompensation were present and during the work-up an intravenous urogram was obtained (Fig. 3*A*). This revealed

a right ectopic kidney with hydronephrosis. The urine showed 25–30 white blood cells per high power field and the patient was referred to the urology service for nephrectomy. The excised specimen (Fig. 3, *A* and *B*) revealed extrarenal calyces, pyelonephritis and arteriolo-nephrosclerosis. The hypertension was only slightly improved, decreasing from 232/118 to 186/92.

Case iv. J.L. This sixty-seven year old white male was admitted to the surgical service of the Veterans Administration Hospital for a possible colon malignancy. Physical examination revealed in the left upper quadrant a palpable mass which was associated with left flank pain radiating to the suprapubic area. The patient was referred to the urology service and an intravenous urogram and retrograde pyelogram demonstrated distortion of the calyceal system suggesting a renal tumor (Fig. 4, *A* and *B*). At surgery a large dark brown mass was found intimately adherent to the kidney. The kidney was removed and examination showed an organized perirenal hematoma of unknown origin. Dissection of the renal pelvis disclosed an extrarenal calyceal system. It was suggested that the perirenal hematoma may have been due to the rupture of an anomalous vein.

Case v. A.H. This fifty-three year old white male was treated on the medical service of the Veterans Administration Hospital for cardiac

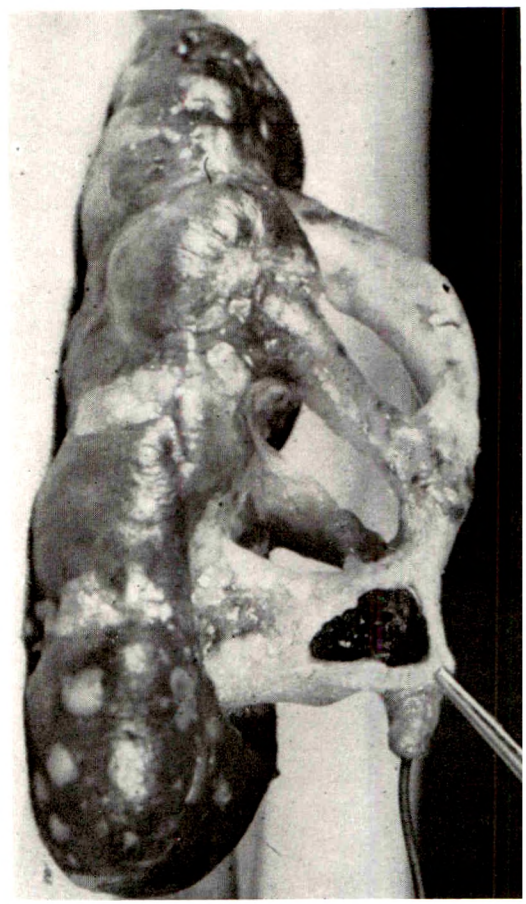


Fig. 2. Case ii. Extrarenal calyces with impacted calculus in the pelvis.

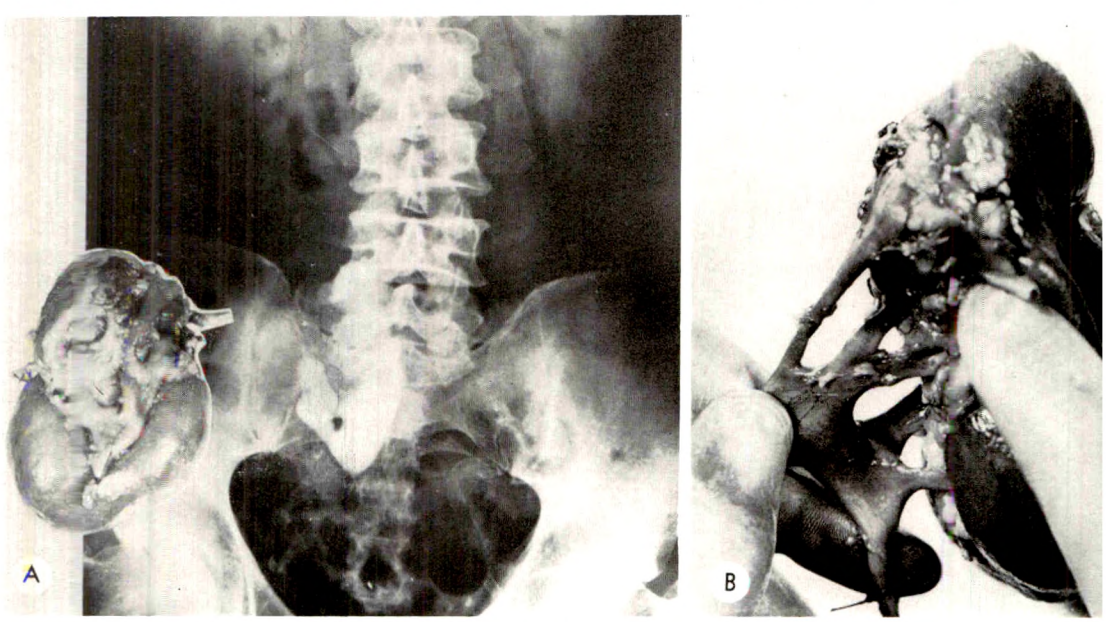


Fig. 3. Case iii. (*A*) Composite photograph of the pyelogram and excised kidney. (*B*) Lateral view showing the extrarenal location of the calyces.

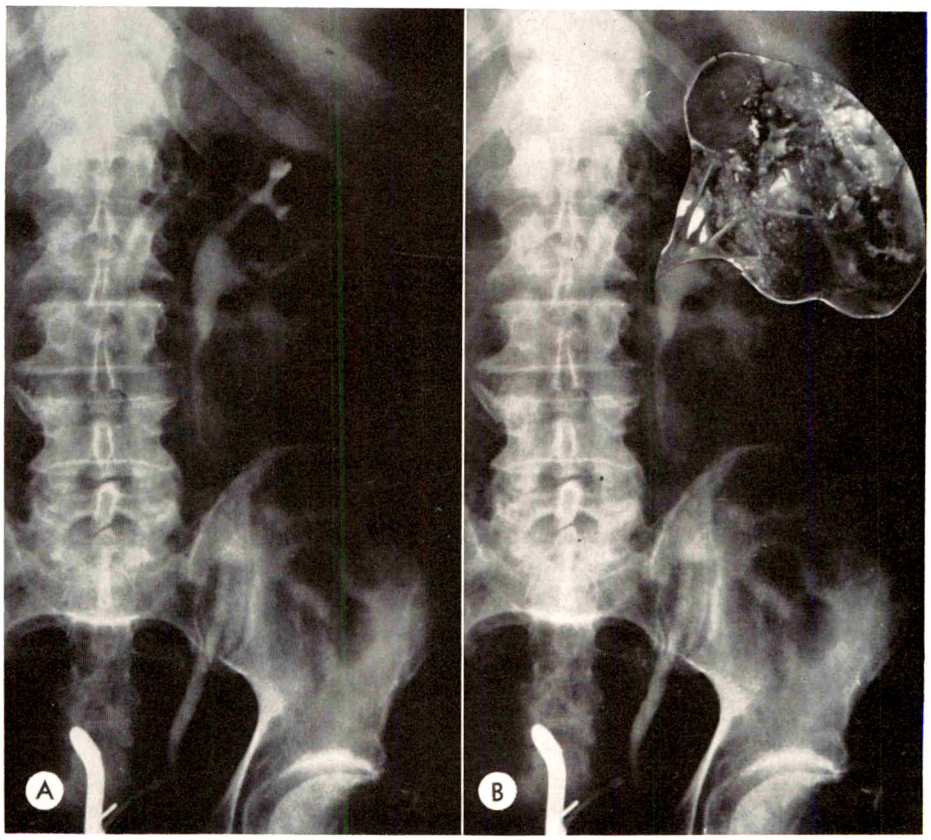


FIG. 4. Case IV. (*A*) Retrograde pyelogram showing deformity of the inferior calyces. (*B*) Composite photograph of the pyelogram and excised kidney.

decompensation secondary to a long history of rheumatic heart disease. Diabetes mellitus was present and there had been an episode of coronary thrombosis in 1955. Urinalyses showed albuminuria, mild pyuria, hyaline and granular casts. The patient expired and at autopsy a bilateral extrarenal calyceal system was found (Fig. 5). In addition, the left kidney exhibited malrotation and was located in an iliac ectopic position.

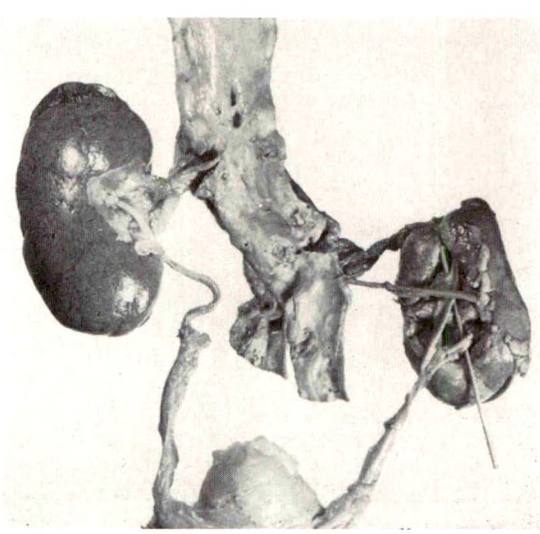


FIG. 5. Case V. Bilateral extrarenal calyces.

CASE VI. E.J. This sixty year old white male was admitted to the Veterans Administration Hospital with a history of gross hematuria of one year's duration. The patient admitted symptoms of prostatic obstruction. Physical examination revealed hypertension and residuals of a cerebral accident in 1957. The prostate was slightly enlarged at palpation and was benign. Urinalysis showed 15–20 red blood cells per high power field. An intravenous urogram and retrograde pyelogram demonstrated distortion of the left calyceal system, suggesting a space occupying lesion (Fig. 6*A*). At this time a diagnosis of extrarenal calyces was made. Surgical exploration disclosed two

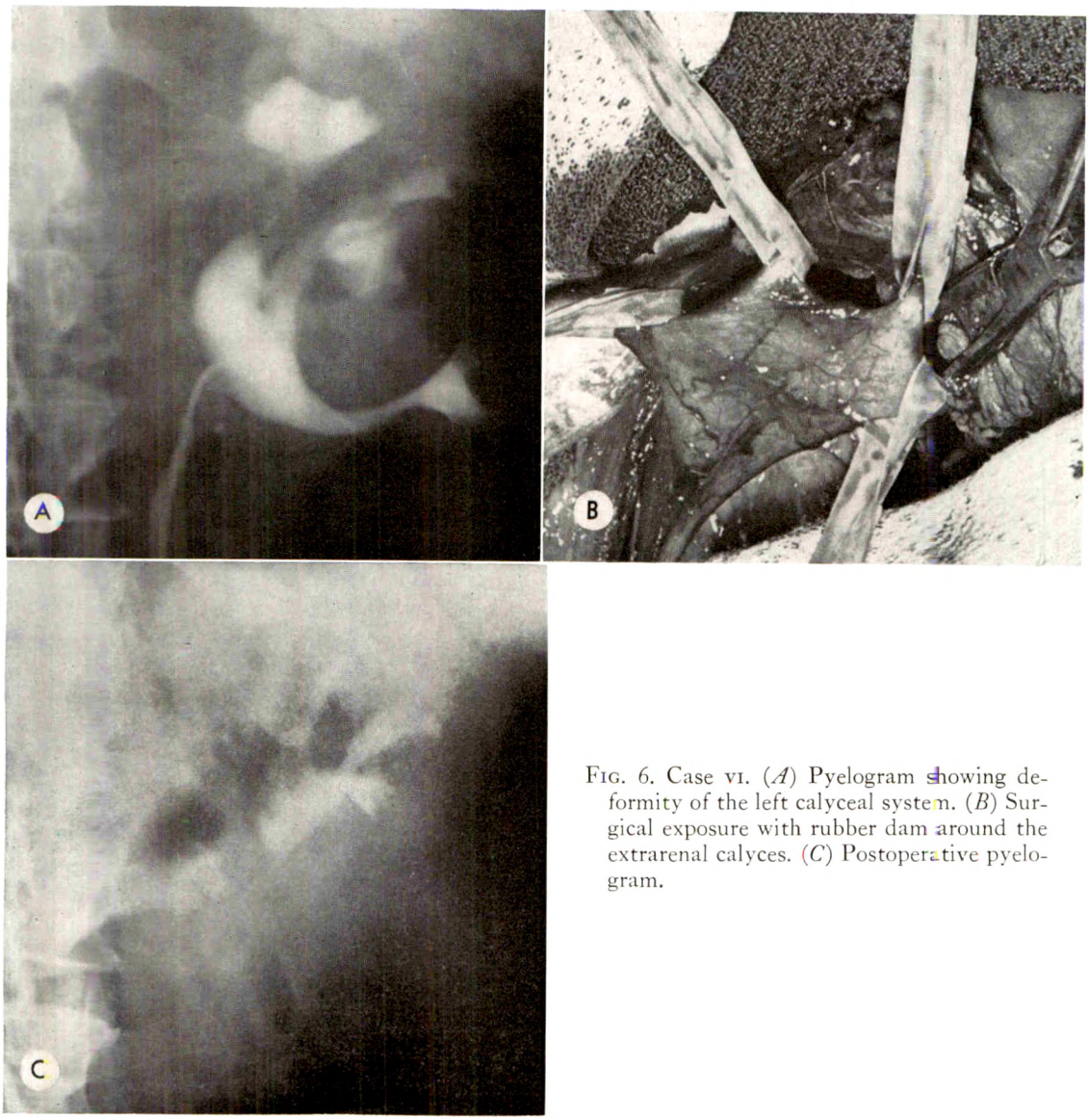


Fig. 6. Case vi. (*A*) Pyelogram showing deformity of the left calyceal system. (*B*) Surgical exposure with rubber dam around the extrarenal calyces. (*C*) Postoperative pyelogram.

large renal cysts and dissection of the renal hilus exposed the pelvis and four major calyces located outside the renal parenchyma, thus confirming the preoperative diagnosis of an extrarenal calyceal system (Fig. 6, *B* and *C*).

Case vii. H.S. This sixty-two year old white obese male was admitted to the Veterans Administration Hospital in 1960 with vague complaints of left flank pain. Urinary symptoms were minimal. An intravenous urogram and retrograde pyelogram revealed a large renal shadow with absence of the superior calyces, suggesting a possible superior pole tumor (Fig. 7). The pyelographic outline of the pelvis and calyces indicated an extrarenal position. Surgical exploration disclosed extensive perirenal lipomatosis and approximately 500 gm. of fat was removed. During the dissection the anticipated extrarenal calyces were identified.

Case viii. W.R. This forty-seven year old white male was admitted to the Veterans Administration Hospital in November, 1957, complaining of severe right flank pain radiating anteriorly and downward to the right lower quadrant. In 1952 a left pyeloplasty had been performed at another hospital. Because of persistent left flank pain, he had entered this hospital in 1953 at which time recurrent hydro-

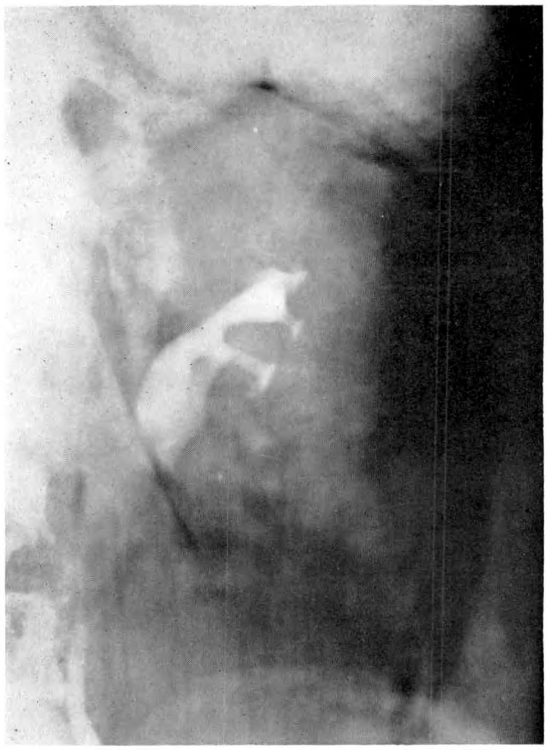


FIG. 7. Case VII. Pyelogram showing a large tumor mass in the upper pole of the kidney, with extrarenal calyces.

nephrosis and a stricture of the ureteropelvic junction were found. A second pyeloplasty was performed with a good result. The patient had no complaints until the onset of the right flank pain three days prior to this admission. Pyelograms showed the presence of a right hydronephrosis due to ureteropelvic obstruction. Surgical exploration revealed extensive peripelvic adhesions and a taut anomalous blood vessel extending to the renal pelvis and kinking the ureteropelvic junction. Further exploration of the hilus demonstrated the presence of extrarenal calyces. No intrinsic stricture of the ureteropelvic junction was found and surgery was limited to resection of the redundant pelvis and division of the aberrant vessel.

COMMENTS

Fourteen cases of extrarenal calyces have been reviewed (Table 1), of which 8 cases occurred in our series. Of the total, 6 cases showed additional congenital abnormalities, namely, ectopia in 4 cases and partial ureteral reduplication in 2 cases. The left side was involved twice as frequently as the right. Renal disease was present in 8 cases and 7 of these could be related to the extrarenal calyceal deformity.

Statistics of renal disease associated with other renal congenital anomalies are not available. However, a kidney featuring a congenital deformity in size, shape, location or formation is known to exhibit a high incidence of renal lesions. The cause may be due to anomalous vessels, fibrous bands, and interference with urinary drainage due to its abnormal position or formation.

The diagnosis of a congenital anomaly is usually made when the clinical symptoms warrant a urologic investigation. In our series, except for the 2 cases found at autopsy, attention was focused on the extrarenal calyceal kidney not because of the anomaly, *per se*, but as a result of clinical symptoms induced by the renal pathology. However, the congenital mal-



FIG. 8. Case VIII. Appearance of the extrarenal pelvis of the kidney prior to the onset of obstructive symptoms.

TABLE I

CASES OF EXTRARENAL CALYCES

Reported by	Other Congenital Anomalies	Location	Renal Disease
Eisendrath[2]		Left	Hydronephrosis
Fürstner[2]	Bifid kidney with hypoplasia	Right	
Herz[2]		Bilateral	Right hydronephrosis
Apert[2]	Bifid kidney	Left	
Veseen[3]		Left	Hydronephrosis
Dunn and Gibson[1]	Ectopia	Left	Hydronephrosis
Malament *et al.*			
Case I A.C.	Ectopia	Right	
II J.M.		Left	Calculous hydronephrosis
III R.B.	Ectopia	Right	
IV J.L.		Left	Perirenal hematoma
V A.H.	Left ectopia	Bilateral	
VI E.J.		Left	Renal cysts
VII H.S.		Left	
VIII W.R.		Right	Hydronephrosis

formation could well have been the cause of the associated renal disease. A good illustration of this is Case VIII, where the patient had been followed with pyelographic studies for several years because of a left hydronephrosis. The right kidney offered little of interest (Fig. 8) and was neglected until the sudden onset of right flank pain revealed an acute hydronephrosis which, on exploration, was found to be due to kinking of the ureteropelvic junction of an extrarenal calyceal system. Consideration must be given to the fact that the multiple elongated infundibula of the extrarenal calyces, exhibiting peristaltic motion in a perirenal area, are more liable to extrinsic influence, as aberrant vessels, and may develop gradual or acute obstruction, as well as other complications.

SUMMARY

Extrarenal calyceal system is a congenital anomaly in which the renal pelvis and calyces lie outside the kidney and are attached to the renal parenchyma at the minor calyceal level.

The diagnosis may be made from routine pyelographic studies when the renal pelvis appears to be situated outside the renal shadow, and the calyces extend to the kidney with an incurvation resembling the prongs of a small hand garden rake.

Of the total of 14 cases reviewed, 8 occurred in our series, indicating that the incidence may be higher than previously suspected. As awareness of this congenital entity increases, more cases may be recognized.

Although extrarenal calyces may exist without causing any clinical symptoms, 50 per cent of the total series exhibited renal disease that could be attributed to this congenital malformation.

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HAMARTOLIPOMA OF THE KIDNEY: CLINICAL AND ROENTGEN FEATURES*

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BECAUSE of the presence of substantial amounts of fat, retroperitoneal tumors containing lipomatous elements can be recognized by roentgen examination. This was originally pointed out by Windholz in 1946.[22] The roentgen features indicating the presence of a retroperitoneal mass have been clearly described by several authors.[3, 4,6,9,11,23] The possibility of roentgenographically distinguishing a lipomatous tumor which arises within the kidney from similar tumors which arise from the retroperitoneal tissues has not been mentioned.

The present report summarizes the roentgen as well as the clinical features in 6 cases of lipomatous tumors arising within the kidney; these cases were collected at this hospital over a period of about nineteen years. It is evident from the small number of cases that this type of lipomatous tumor is uncommon. We believe, however, that it is of considerable clinical importance to separate lipomatous tumors arising within the kidney from other retroperitioneal tumors. This opinion is based, not only on the features of the current group of cases, but also on a review of the literature, which indicates that there is no documented case of an intrarenal lipomatous tumor which has metastasized.

REVIEW OF THE LITERATURE

In Robertson and Hand's[16] 2 personal cases and their summary of 12 cases from the literature, there was no example of a malignant lesion. In Klapproth, Poutasse and Hazard's[10] series of 4 personal cases and 12 analyzed from the literature, none were considered to be malignant. Williams and Savage[21] reported 1 personal case without metastases and reviewed 29 others from the literature. These latter authors considered all of these tumors to be "liposarcomas" of the kidney on the basis of histologic appearance and the presence of metastases in 2 cases, 1 reported by Tesler and Koiransky[19] and the other by Lubarsch as quoted by Pemberton and MacCaughan.[15] However, the case of Tesler and Koiransky[19] is clearly stated by the authors to be perirenal in origin and the case of Lubarsch is referred to by Pemberton and Mac Caughan[15] as also being perirenal.

Histologic criteria of malignancy based on the appearance of individual cells are uncertain. Vascular or lymphatic invasion has not been described. The fact that the capsule of the kidney may be penetrated by the tumor is not sufficient evidence of the malignant nature of these neoplasms. In 2 cases from this institution previously reported by Edelman[5] and brought up to date in this report (Cases 1 and 11), the designation "liposarcoma" was originally used on the basis of extension into the perirenal soft tissues. These patients have survived fourteen and nineteen years since nephrectomy without evidence of disease. Review of the histologic slides indicates no microscopic features to warrant the diagnosis of a sarcoma. In the series of 29 cases reviewed by Williams and Savage,[21] 11 patients were followed for more than one year without evidence of recurrence or metastasis. Survival for more than ten years was not uncommon in this series.

For practical purposes, therefore, it would appear that lipomatous tumors arising within the kidney are benign and that permanent cure may be anticipated if complete resection is feasible.

TERMINOLOGY

From the pathogenetic point of view, an

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unequivocal classification or designation of lipomatous tumors of the kidney is difficult and not generally agreed upon. In addition to substantial amounts of fat, these tumors usually contain smooth muscle elements and are often rich in blood vessels as well. As a result of their "mixed" character, such tumors have been variously designated as lipoma or angiolipomata,[16] fibrolipomata, angiofibrolipomata, etc.[2,10,12,13,17,18] Masses or tumors of exactly the same histologic and gross characteristics are not infrequently seen in patients with tuberous sclerosis[1,7,8,14] and in such instances have been referred to as hamartomata. According to Robertson and Hand,[16] careful search at necropsy indicates that small "lipomata" are found in about 1 per cent of all cases and are often multiple. Somewhat similar lesions within the liver have also been referred to as hamartomatas. On the basis that it is likely that lipomatous tumors of the kidney arise from congenital rests, the term "hamartolipoma" has been used in the title of this report. It should be emphasized that most patients with this tumor do not suffer from tuberous sclerosis. The designation hamartolipoma also serves to suggest the important clinical features of these tumors, namely, slow growth and benign nature. From the pure histologic point of view, however, the most suitable designation for these tumors is myolipoma or angiomyolipoma.

PATHOLOGY

In the early stages, a hamartolipoma of the kidney is entirely confined to the kidney parenchyma and is sharply demarcated from the normal kidney tissue. In places, a thin pseudocapsule may be evident but it is ordinarily not possible to enucleate the tumor cleanly from the kidney.

The fact that growth may be extremely slow is indicated by a case reported by Klapproth *et al.*[10] During a period of seventeen years, this patient complained of recurrent painless hematuria. When a lipomatous tumor was removed, it was only 1 cm. in diameter. Such tumors may, however, reach a huge size and one has been reported which attained a weight of 3,500 gm.[21] With growth of the tumor, there is usually compression and resultant deformity of the collecting system of the kidney. Rarely, if ever, is there direct infiltration into the pelvis or the calyces. More commonly, growth of the tumor is peripheral, into and through the renal capsule, but even in such instances the adherent and infiltrated capsule can ordinarily be identified.

In many cases, satellite nodules of similar character may occur within the kidney substance at some distance from the main tumor. The presence of more than one tumor within the kidney has sometimes been interpreted as evidence of local metastases[12,21] but it seems equally likely that a multicentric origin is the cause of this finding.

CLINICAL FEATURES

In the absence of tuberous sclerosis, hamartolipomas of the kidney are most commonly evident in the third to the fifth decades. It is frequent to obtain a history of a mass being present and growing slowly for several years prior to the time of surgical intervention. According to the literature, in the majority of instances, these tumors are detected as incidental findings because of the presence of a mass on abdominal palpation. In other cases, the patient presents with a history of an episode or episodes of rather acute flank or abdominal pain. This was true in 5 of the 6 cases included in this report. In such cases, operative intervention has demonstrated hemorrhage within or around the tumor or kidney which presumably was the cause of the pain. Hemorrhage or hematoma formation of this type is usually seen in the absence of any history of significant trauma.

The fact that hemorrhage is common is of importance to the radiologist because the characteristic roentgen feature of large lucent areas within a tumor mass may be partly obscured by the blood. Moreover,

perinephric hematoma formation may show all the roentgen features of a perinephric abscess. Hematuria is not a common finding. It was present in only 1 patient in the 6 cases described in this report.

In all reported series, the incidence in females is greater than in males by 2 or 3 to 1. Of the 6 cases included in this report, all were females.

These tumors are bilateral in a significant number of cases, perhaps about 10 per cent.[21] In 2 of the 6 cases described below, the tumors were bilateral. This feature is of great clinical importance and must be carefully investigated in every case, since these tumors are difficult to eradicate without nephrectomy. If further experience should confirm the opinion that these tumors do not metastasize, it would appear to be reasonable not to risk the loss of normal renal tissue by attempting operative intervention on either side when bilateral tumors are present. In such cases, it is likely that both kidneys will eventually be completely destroyed and the patient will die of uremia, but this is not likely to occur for many years.

REPORT OF CASES

CASE I. I.E. This was a forty-one year old female admitted in 1946 with the chief complaint of sharp intermittent pain in the left lower quadrant of two days' duration. The pain was accompanied by nausea and vomiting and radiated toward the back. There was a history of low back pain for a period of about thirteen years.

Physical examination was negative except for the presence of a large tender mass in the left flank and moderate costovertebral angle tenderness. Hemoglobin was 75 per cent, white blood cell count 8,600 cells per ml., with a normal differential count. Urine examination was not remarkable. Blood urea was not elevated. Intravenous pyelography was reported as showing distortion of the calyces in the upper pole of the left kidney. This was confirmed by retrograde pyelography. The appearance was described as characteristic of a renal neoplasm. A left nephrectomy was performed a few days after admission with the preoperative diagnosis of hypernephroma.

The specimen consisted of the kidney and the investing Gerota's fascia. A considerable amount of blood was present in the adherent perirenal soft tissues. The kidney weighed 450 gm. and appeared to be enlarged and markedly deformed. The lower two-thirds of the kidney was replaced by a sharply circumscribed encapsulated tumor about 12 cm. in length. The capsule of the kidney could easily be stripped except at the area of bulging of the tumor. On section, a markedly yellow tumor was found which surrounded and distorted the lower portion of the pelvis and the lower calyces; the upper third of the kidney appeared normal.

Histologic diagnosis was originally a leiomyoliposarcoma. The patient is alive and well fourteen years after nephrectomy. The pathologist has reviewed the slides and has changed the diagnosis to a benign tumor.

Comment: This patient is entirely well fourteen years after nephrectomy for an intrarenal lipomatous tumor. The tumor was discovered because of an acute episode of pain, although "low back pain" had been present for many years. A perirenal hematoma was found at exploration. The original pyelograms of this case are not available for review. It is likely, however, in view of the operative findings, that lucent areas within the tumor might have been evident on careful search.

CASE II. S.M. This was a forty-six year old female admitted to this hospital in 1941 for exploration of a left flank mass known to have been present for at least two years. It had been discovered during examination after an automobile accident. There had been no evident increase in the size of the mass during the two year period of observation. Intravenous pyelography performed one year prior to admission demonstrated that the mass was in the left kidney and had compressed and distorted the inferior and middle calyces.

Physical examination at the time of admission was negative except for a grapefruit-sized mass in the left flank, which was ballotable but not tender. A plain roentgenogram of the abdomen did not show a distinct left renal outline (Fig. 1*a*). Intravenous pyelography again demonstrated compression and elevation of the middle infundibulum as well as the lower portion of the pelvis of the kidney (Fig. 1*b*). A

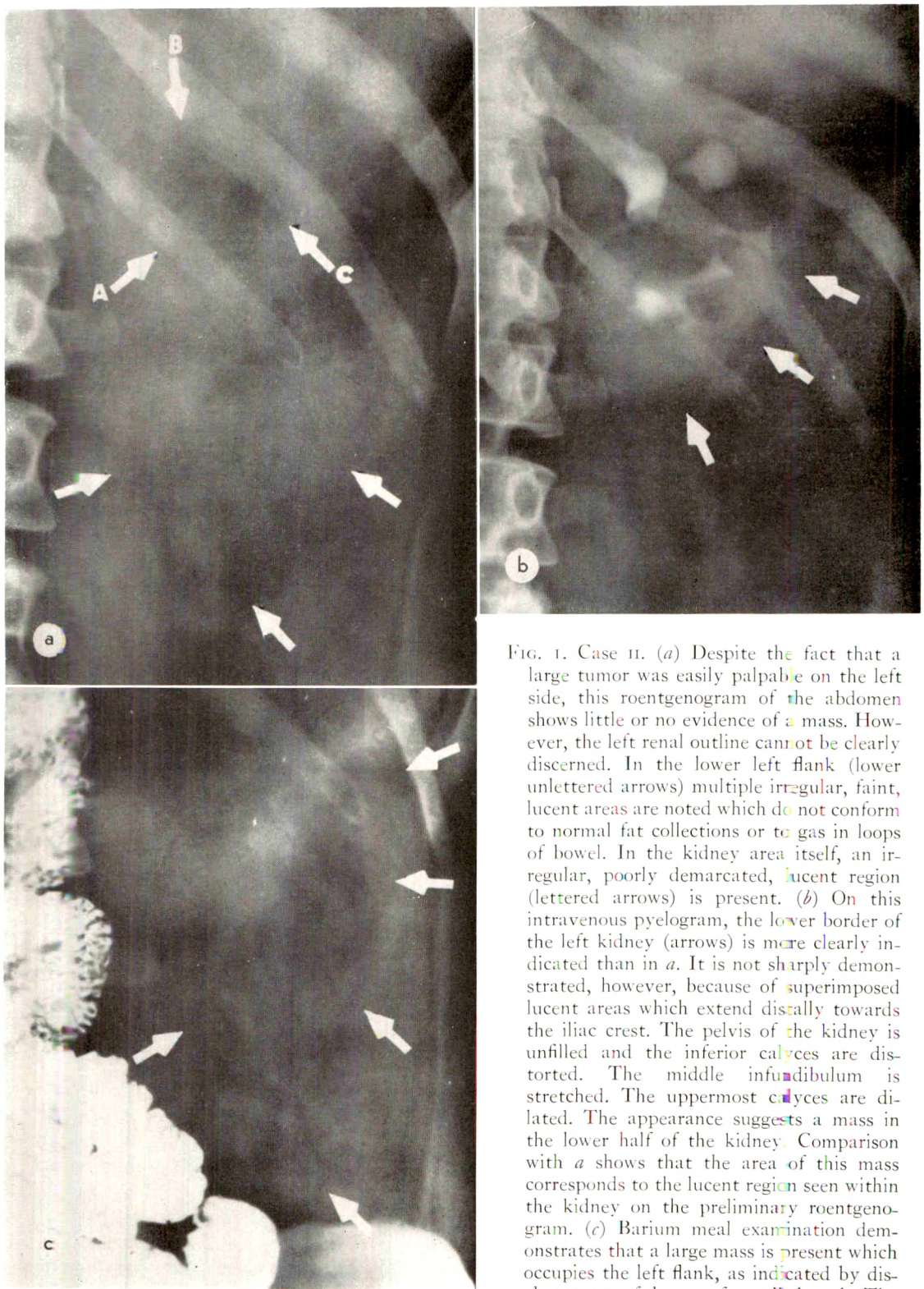


Fig. 1. Case II. (*a*) Despite the fact that a large tumor was easily palpable on the left side, this roentgenogram of the abdomen shows little or no evidence of a mass. However, the left renal outline cannot be clearly discerned. In the lower left flank (lower unlettered arrows) multiple irregular, faint, lucent areas are noted which do not conform to normal fat collections or to gas in loops of bowel. In the kidney area itself, an irregular, poorly demarcated, lucent region (lettered arrows) is present. (*b*) On this intravenous pyelogram, the lower border of the left kidney (arrows) is more clearly indicated than in *a*. It is not sharply demonstrated, however, because of superimposed lucent areas which extend distally towards the iliac crest. The pelvis of the kidney is unfilled and the inferior calyces are distorted. The middle infundibulum is stretched. The uppermost calyces are dilated. The appearance suggests a mass in the lower half of the kidney. Comparison with *a* shows that the area of this mass corresponds to the lucent region seen within the kidney on the preliminary roentgenogram. (*c*) Barium meal examination demonstrates that a large mass is present which occupies the left flank, as indicated by displacement of loops of small bowel. The numerous partially confluent lucent areas (arrows) are more clearly shown in this reproduction. These extend into the kidney substance.

barium meal examination (Fig. 1*c*) showed marked displacement of the jejunal loops toward the midline. A left nephrectomy was performed.

In the posterior aspect of the kidney were several masses, the largest of which measured 12 cm. in diameter. These masses appeared to be well demarcated from the kidney parenchyma and the portions that extended outward from the kidney were clearly delineated by a thin-walled translucent, in places hemorrhagic, capsule. On cut section, it was found to be soft and uniformly golden-yellow except for a large 3.5×3.5 cm. area near the kidney surface which was grayish-yellow and firmer in consistency. The pelvis of the kidney was compressed by the mass. A large portion of normal kidney was preserved.

The histologic diagnosis was lipomyosarcoma of the kidney but the pathologist included in his report the observation that the diagnosis of sarcoma was based on what was presumed to be an infiltrating character of the tumor as described by the surgeon.

Comment: In this patient, an asymptomatic mass in the left kidney was discovered incidentally and did not change in size in a period of two years. This patient is alive and well nineteen years after nephrectomy. Review of the original roentgenograms shows lipomatous, *i.e.*, lucent areas, within the confines of the kidney tumor (Fig. 1, *a*, *b* and *c*).

CASE III. B.S. This twenty-four year old female was admitted with the chief complaint of a painful mass in the right flank. This mass, noticed by the patient herself six months prior to admission, was said to have increased recently in size. Originally, the mass was not painful or tender. However, seven days prior to admission, she began to complain of pain on the right side of the abdomen which radiated to the back. The pain increased in severity and was accompanied by nausea and rigidity of the right side of the abdomen. Within a period of four hours, however, the pain diminished. She was hospitalized elsewhere and it is known that the urine examination at that time showed no evidence of blood. Five days prior to admission to this hospital, she showed temperature increases to 101° F. She received a blood transfusion one day prior to admission.

On admission, physical examination was negative except for a grapefruit-sized mass in the right upper and lower quadrants. The mass was smooth and not tender. Laboratory examination showed a hemoglobin of 13.5 gm. per 100 cc., a white blood cell count of 4,500 cells per ml. with a shift to the left. The urine was negative. Cystoscopy was within normal limits. Barium enema examination and gallbladder study were negative except for marked caudad displacement of the hepatic flexure. Retrograde pyelography (Fig. 2) revealed the collecting system of the right kidney to be displaced towards the midline. In the kidney and immediately adjacent to the pelvis, multiple partially confluent lucent areas were evident. The right psoas margin could not be identified. There was a minimal scoliosis of the lumbar spine with convexity to the left. The presence of the lucent areas replacing the kidney parenchyma led to the preoperative

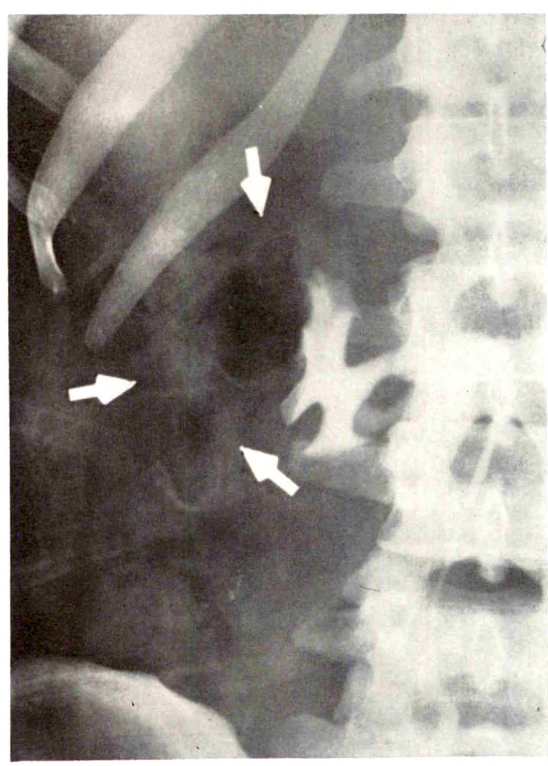


FIG. 2. Case III. Right retrograde pyelogram. The renal outline cannot be discerned. The renal shadow is partially occupied by irregular lucent areas (arrows) which extend to the collecting system. The calyces are blunted or flattened. The collecting system and ureter are displaced towards the midline. The psoas margin is obliterated.

diagnosis of a lipomatous tumor of the kidney. Laparotomy revealed a large mass arising from the right kidney and displacing the hepatic flexure downward. A smaller mass of similar consistency was felt in the left kidney. A right nephrectomy was performed.

The specimen showed a large subcapsular hemorrhage in the upper pole. Under the hemorrhage, there was a mass about 7 cm. in diameter in the substance of the kidney. It was yellow in color with several grayish-pink, firm areas within it. A number of yellowish satellite masses were scattered throughout the remaining portion of the kidney. The renal pelvis appeared normal.

The histologic diagnosis was multiple myolipomata of the kidney.

Comment: At operation in this patient, there was evidence on palpation of a soft, small mass in the left kidney in addition to the large tumor of the right kidney. This is presumed also to be lipomatous. The roentgenogram of the abdomen taken during right retrograde pyelography shows no definite lucent areas within the left kidney outline (Fig. 2). The patient's history of recent pain and increase in size of the mass may be attributed to the subcapsular hematoma found at operation. This patient is alive and well one year after discharge.

Case iv. L.L. This fifty-one year old female was admitted with the chief complaint of right flank pain of five days' duration. The history revealed intermittent episodes of left renal colic for the preceding six years.

Physical examination was negative except for a tender mass in the right flank. Laboratory examination revealed a hemoglobin of 9.6 gm. per 100 cc. and a white blood cell count of 7,550 cells per ml. with a normal differential count. The urine analysis was normal. Sedimentation time was 100 mm. per hour. A plain roentgenogram of the abdomen showed obliteration of the right psoas outline and a moderate scoliosis of the lumbar spine. The kidney outline was obscured but appeared to be considerably enlarged. Intravenous pyelography revealed a moderate medial displacement of the collecting system of the right kidney and marked deformity and compression of the superior calyx and infundibulum (Fig. 3*a*). The diagnosis of a perinephric collection, presumably blood because of anemia, was made. At operation, a tense blueish mass was found in the right flank near the upper pole of the kidney. Nephectomy was performed.

The specimen showed a mass 5×5 cm. within the upper pole of the kidney with areas of fat and hemorrhage. There was a large subcapsular hematoma. The lower two-thirds of the kidney was normal.

Histologic diagnosis was myolipoma with subcapsular hematoma. This patient died two years after nephrectomy from a coronary occlusion. Autopsy was not obtained. There had been no complaints referable to the urinary tracts since the time of operation.

Comment: Careful retrospective examination of the intravenous pyelogram of this patient shows a faint lucent area adjacent to the deformed superior infundibulum and calyx (Fig. 3*a*). This was somewhat better seen on a roentgenogram of the abdomen taken six years previously (Fig. 3*b*) during an episode of left renal colic due to a small calculus. It is likely that the hemorrhages within the tumor as well as the subcapsular hematoma served to obscure the fatty areas.

Case v. G.S. This twenty-nine year old female was admitted with the chief complaint of right flank pain of three weeks' duration. The pain started suddenly with radiation to the right shoulder while the patient was working in the office and necessitated morphine injection. There was no hematuria or previous significant history. Two weeks prior to the onset of the severe pain, because of vague abdominal symptoms, she had had a gallbladder series which was said to have shown stones.

Physical examination on admission was negative except for a large mass in the right flank. Hemoglobin was 9.4 gm. per 100 cc. White blood cell count was 12,700 per ml. with a shift to the left. Urine was negative. Intravenous pyelography (Fig. 4*a*) revealed somewhat diminished function on the right. The pelvis and calyces were stretched and appeared to be uniformly narrowed and displaced toward the midline. The renal outline could not be discerned. In retrospect, numerous lucent areas can be seen within the kidney area and extending inferiorly towards the iliac crest. The most marked deformity of the collecting system was

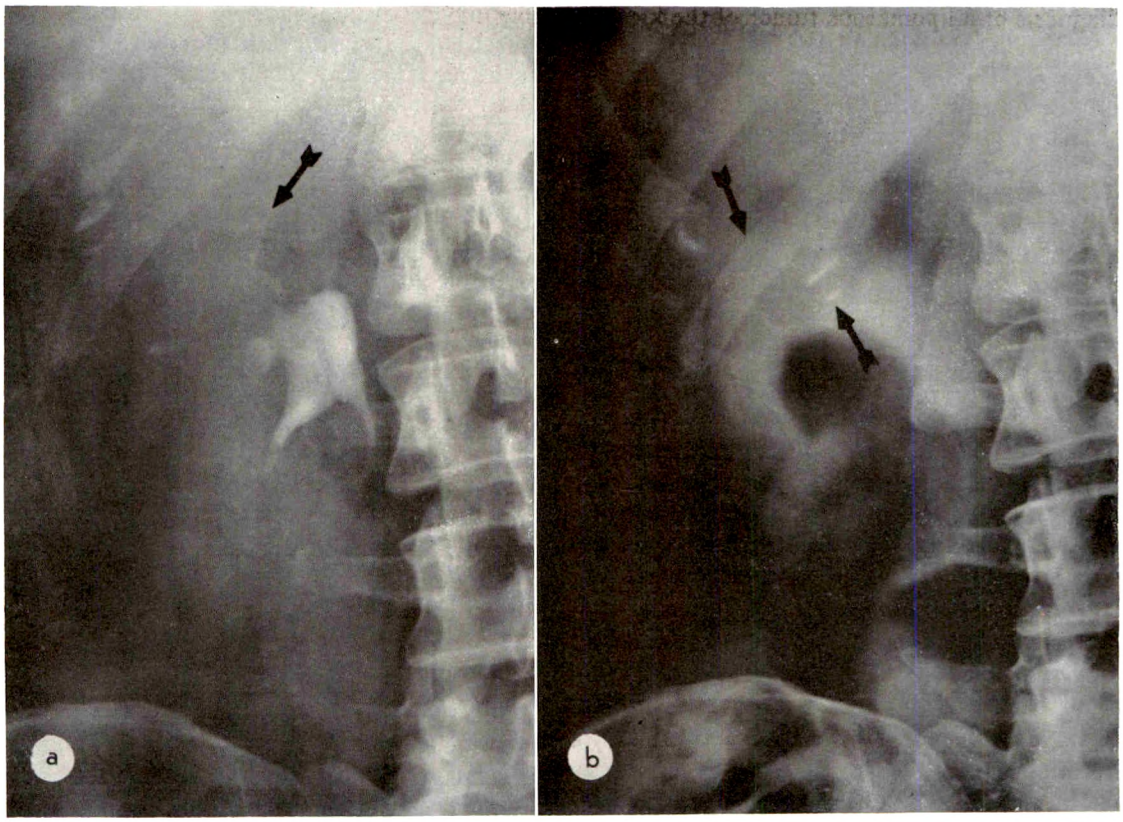


FIG. 3. Case IV. (*a*) Intravenous pyelogram shows displacement of the right renal pelvis towards the midline. The superior infundibulum and calyx (arrow) are narrowed and deformed. The renal outline and psoas margin are obscured. On the original roentgenogram, a faint lucent area can be discerned adjacent to the deformed superior calyx. At operation, an intrarenal lipoma with numerous hemorrhagic areas was found in addition to a large subcapsular hematoma. (*b*) Roentgenogram taken six years before *a* because of left renal colic due to a ureteral stone. A faint lucent zone (between arrows) about 1½ inches in diameter can be discerned within the upper pole of the right kidney. The outline of the kidney is clearly evident at this time.

an inferior prolongation and stretching of the lowermost infundibulum. The significance of these roentgen findings or the significance of somewhat similar lucent areas within the outline of the left kidney was not appreciated preoperatively. After preparation with multiple transfusions, the patient was explored and a right nephrectomy was performed.

The specimen consisted of a kidney weighing 1,375 gm. and measuring 23×9.5×5 cm. The surface of the kidney was lobulated but the reniform shape was retained. The capsule was stripped with difficulty and revealed a grayish-red surface showing numerous yellowish nodules varying in size from 3 mm. to 9 cm. The largest of these masses occupied the lower pole of the kidney. A section of the kidney revealed it to consist of numerous yellowish, glistening, fleshy nodules and hemorrhagic cystic areas filled with blood clot. There were only small areas of residual renal parenchyma; within these areas tiny yellow nodules were also noted. There was no evidence of invasion of the ureter, renal pelvis or major branches of the renal artery and veins.

Histologically, the tumor was a myolipoma with no evidence of malignancy.

As a result of the findings, the pyelograms were reviewed and attention was called to the lucencies in the left kidney. Careful palpation of the left renal area confirmed the presence of a mass. Three months after the first operation, the patient was readmitted and intravenous pyelography was repeated. There was dilatation of the pelvis and calyces of the left kidney (Fig. 4*b*), which, however, did not appear to be remarkably distorted or compressed. Only

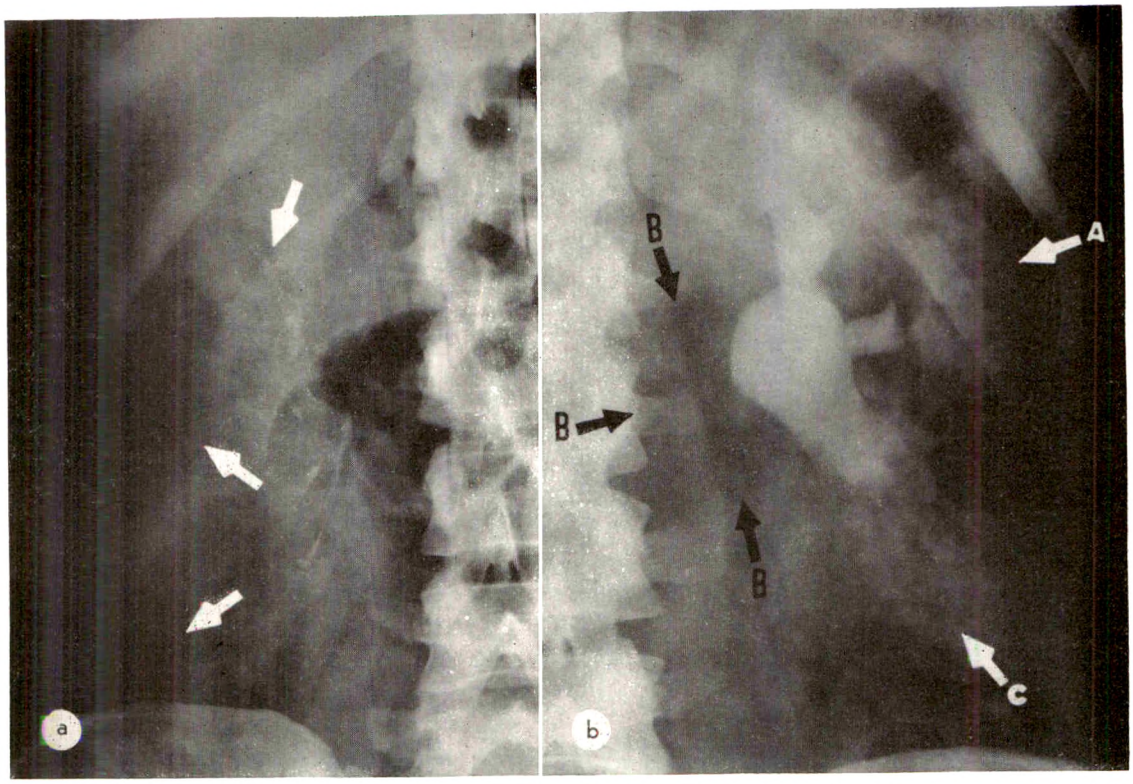


Fig. 4. Case v (*a*) Intravenous pyelogram shows compression of the entire collecting system of the right kidney. The kidney outline is absent. Numerous band-like and more globular lucent areas (arrows) with intervening areas of water density occupy the renal area and extend inferiorly. (*b*) Intravenous pyelogram three months after right nephrectomy shows moderate dilatation of the left pelvis and calyces. Only the upper lateral portion of the kidney outline (arrow A) is clearly demarcated from adjacent normal perirenal fat. Within the lower two-thirds of the kidney, there are numerous discrete and confluent lucent areas which replace the normal renal outline and extend inferiorly toward the iliac crest (arrow A to arrow C). Medially, adjacent to the pelvis (arrows B), there is a more discrete globular lucent area which extends to the spine.

the upper portion of the lateral part of the left renal outline could be identified. The lower pole was completely obliterated or effaced by an irregular, mottled, poorly demarcated group of shadows with many lucent areas within it. Apparently located medial to the pelvis of the kidney there was a somewhat more discrete, lucent, ovoid area with streaks of water density within it. The left renal area was explored and a mass was found within the kidney extending into the adjacent soft tissues. It was clear, however, that this tumor could not be removed without removing the kidney. As a result, only a biopsy was performed. The biopsy was reported as myolipoma. Postoperatively, the patient bled briskly from the wound. This was brought under control, but ten days after discharge from the hospital rather massive bleeding recurred and the patient died.

Comment: This patient demonstrates the difficult clinical problem when renal lipomata are bilateral. In retrospect, it would have been wiser not to have explored the second kidney to determine the possibility of removal. In fact, it can be argued that, if the status had been correctly evaluated, neither kidney should have been explored.

Case vi. L.G. This was a fifty-two year old female who entered the hospital with the chief complaint of pain in the left flank. There was no history of hematuria.

Physical examination was negative except for a ballotable and slightly tender mass in the left flank. Blood pressure was 130/70. Laboratory examination showed a hemoglobin of 9.6 gm., a white blood cell count of 12,400 per ml. with a slight shift to the left. Urine examina-

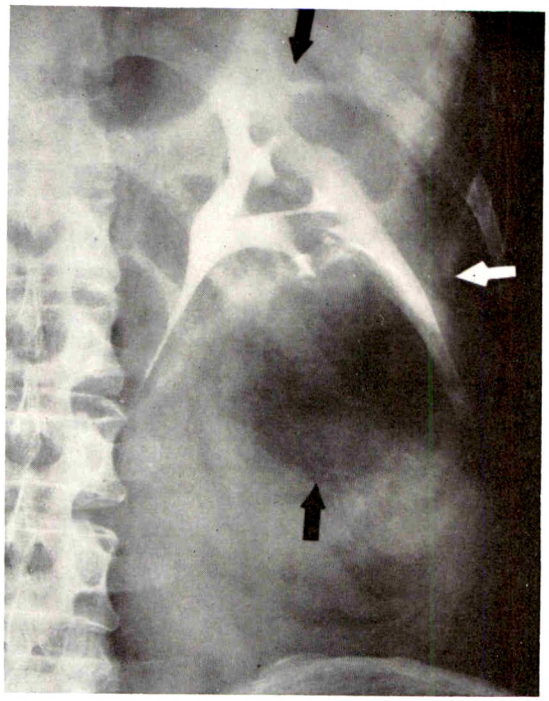


FIG. 5. Case VI. Intravenous pyelogram shows elevation of the collecting system and stretching of the inferior calyces. Only the superior lateral margin of the kidney outline (upper arrow) is evident. Within the lower pole of the kidney, a globular lucent zone (lower arrows) is present which is capped inferiorly by a large crescentic area of water density. The psoas margin can be faintly seen through the mass.

tion was not remarkable. Sedimentation time was 4 mm. in the first hour. Roentgenography of the abdomen and intravenous pyelography (Fig. 5) showed a mass in the lower pole of the left kidney. There was displacement and distortion of the lowermost calyces. The renal outline of the lower half of the kidney could not be seen. Within the lower pole of the kidney, there was a very poorly demarcated, markedly lucent, somewhat spherical lesion with faint, somewhat beaded, linear densities extending through it. At operation, the presence of a mass in the lower pole of the left kidney was confirmed and nephrectomy was performed.

The specimen showed a rather soft mass about 12 cm. in diameter. It was well circumscribed, was entirely within the kidney parenchyma and contained areas of necrosis and hemorrhage. In discrete areas, distinct yellowish fat was discernible.

Histologic report was myolipoma of the kidney. There was no evidence of any malignant change. The patient is alive and well four years after nephrectomy.

Comment: The roentgen features (Fig. 5) in this case correspond exactly to the anatomic findings, since this lesion was discrete and was confined to the kidney.

ROENTGEN FEATURES

The roentgen features of lipomata of the kidney may be divided into two groups: (1) findings indicative of a mass and (2) findings indicative of fatty tissue within the mass. The first group includes deformity and compression of the kidney pelvis and calyces characteristic of any intrarenal mass (Fig. 1*b*). In the case of a lipoma, invasion of the collecting system and bizarre deformities are unlikely. Displacement of the pelvis and calyces as a whole (Fig. 2 and 5) is a more common finding in a lipomatous tumor than in a hypernephroma, presumably because of its slow growth. This generalized displacement of the collecting system may be quite marked in the larger tumors when extrinsic growth is extensive. In such cases, there may also be obvious displacement of adjacent small bowel loops (Fig. 1*c*) and colon.

The presence of a renal lipomatous tumor which, clinically, is easily palpable may be completely overlooked roentgenologically unless pyelography is performed. Moreover, if attention is given exclusively to the deformed collecting system, the extent of the tumor will usually be underestimated. The reason for this is that the usual roentgen feature of a large kidney mass, that is, a uniformly dense globular area continuous with but protruding from the kidney outline, is absent. Since a lipomatous tumor has a decreased density, the kidney outline is completely lost or markedly obscured at the site of the tumor (Fig. 1*b*, 2, 4*a*, 4*b*, and 5). Moreover, no clear-cut periphery of soft tissue or water density is present outlining the limits of the tumor. Instead, a nondemarcated, nondescript, mottled shadow consisting of irregular lucent zones interspersed with

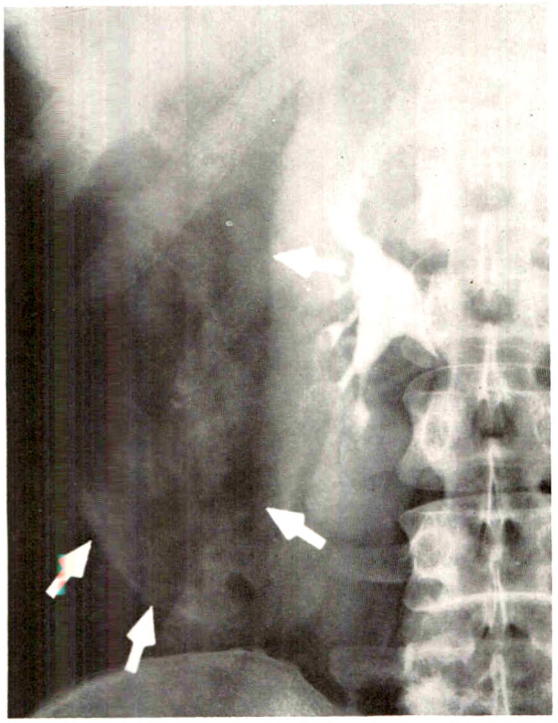


Fig. 6. Perirenal lipoma. The sharply outlined lateral aspect of the kidney is compressed and straightened (medial arrows). The kidney is elongated and displaced toward the midline. The pelvis and calyces are within normal limits. A mass composed of mottled lucent areas is immediately adjacent to the kidney. The lower margin of the tumor is demarcated by a capsule of water density (lower two arrows) from the adjacent normally homogeneous retroperitoneal fat.

equally irregular areas of water density is present (Fig. 1*c*, 2, and 4, *a* and *b*). The lucent areas may be quite obvious (Fig. 2 and 5) but frequently they are so faint that intentional and careful search for them must be made. It may be necessary to repeat the roentgenographic study with better technique before the appearance is convincing. In most instances, the configuration of the lucent areas has no resemblance to gas in the bowel. Moreover, a gas filled portion of the bowel shows considerably greater lucency than a collection of fat of similar size. If there is any question, repeat examination including oblique views will demonstrate the constancy of the lucent areas and confirm their relationship to the kidney or retroperitoneal area.

Theoretically, laminagraphy should also be useful for this purpose. In those cases in which the lucent areas are immediately adjacent to the pelvis and calyces (Fig. 2 and 5), there can be little doubt of the intrarenal location of the tumor. Unfortunately, even in such instances, hemorrhage within the tumor may obscure the original lucent zone (Fig. 3, *a* and *b*). Further diagnostic difficulty may arise as a result of perirenal hemorrhage which may exactly simulate, roentgenologically, a perinephric abscess.

In contrast to an intrarenal lipomatous tumor, a retroperitoneal tumor containing fat rarely shows evidence of extension into the kidney substance or deformity of the pelvis or calyces indicative of an intrinsic mass. There may be extrinsic compression of the kidney or marked dislocation of this organ as a whole. A distinction can sometimes be made between a perirenal lipomatous tumor (Fig. 6) and a similar tumor arising elesewhere in the retroperitoneal tissues on the basis of the location of the mass. Perirenal lipomatous tumors may have a somewhat better prognosis than other retroperitoneal tumors because complete excision is more likely to be feasible.

Renal lipomata must also be distinguished from renal replacement lipomatosis. This condition is usually associated with inflammatory disease and contraction of the kidney such as occurs in calculous pyelonephritis. Excess inflamed fat is found within the hilus of the kidney as well as surrounding the kidney. The outer aspects of the opacified pelvis and calyces may be rather uniformly outlined by such fat deposits. Recognition of the more uniform distribution of this fat and the basic underlying disease serve to differentiate this condition from a lipomatous tumor.

Since lipomata of the kidney may be multiple and bilateral, the deformity of the pelvis and calyces may simulate polycystic kidneys.[10] It is essential in such cases to recognize the numerous lucent zones indicative of the presence of fat within the masses.

There are 4 cases of hamartolipomata of the kidney reported in the literature[10,13,20,21] in which aortography was utilized for diagnostic purposes. Puddling of the opaque material as well as vascular displacements were demonstrated which resembled the findings seen with hypernephromata. It would seem, therefore, that this is not a useful technique for differential diagnosis in such instances.

SUMMARY

Lipomatous tumors of the kidney are uncommon lesions. Their true incidence is difficult to establish because of confusion in terminology. Such tumors have been variously designated as lipomata, liposarcomata, angiolipomata, leiomyolipomata, angiofibrolipomata nephrolipomata, and hamartomata. Histologically, the term "myolipoma"seems most apt, since muscle elements as well as fat are present. Pathogenetically, the term hamartolipoma appears most suitable, since it is likely that such tumors arise from embryonic rests.

A review of the literature as well as the features of the reported group of cases indicates that lipomatous tumors of the kidney are benign. There is no documented case which has shown evidence of metastases. For this reason, it is of clinical importance to distinguish this type of tumor from similar or mixed retroperitoneal tumors, which metastasize in a significant number of cases. Moreover, complete surgical removal of an intrarenal lipoma is usually less difficult than removal of a retroperitoneal tumor.

Six cases of renal hamartolipomata are presented in this report. In 5, the presenting symptom was a painful mass. All cases were in females. None suffered from tuberous sclerosis. In 2 cases, bilateral tumors were present. All patients were operated upon. Four are alive and well nineteen, fourteen, four and one year after surgery. One patient died subsequent to exploration of the left kidney after right nephrectomy, and the sixth from coronary occlusion.

The roentgen features of renal lipomata are usually sufficiently clear-cut to warrant a correct preoperative diagnosis. The diagnosis is based on the demonstration of a mass within the kidney containing lucent, *i.e.*, fatty, areas.

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PULMONARY HAMARTOMA*

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ALTHOUGH, according to Bateson and Abbott,[1] only 253 cases of pulmonary hamartoma were on record up to October, 1960, the literature is now so comprehensive that it seems superfluous to survey the history and the gross, microscopic, and usual roentgen findings of the lesion.

The object of the present paper is to report an additional 10 cases which differ in various ways from the series published so far.

All the patients were operated upon in the Departments of Thoracic Surgery of the University Hospital, Copenhagen, during the period 1951–1960, and the diagnosis was confirmed histologically in each case.

REPORT OF CASES

CASE I (Fig. 1, *A* and *B*). A female, aged five, with a history of operation for hiatal hernia at the age of three. After the operation, she thrived but continued having attacks of vomiting. Follow-up roentgen examination of the esophagus two years later showed a rounded well-defined, large mass located basally in the left lung, behind the heart, and unrelated to the esophagus. There was no visible calcification within the contours of the lesion. Left sided thoracotomy was performed. Posteriorly in the lower lobe, a firm, nodular tumor the size of a tangerine was palpable. Lobectomy and herniotomy were done and the postoperative course was uneventful. Gross and microscopic study revealed a typical hamartoma.

CASE II (Fig. 2). A male, aged fifty-six, who had always been in good health. At a routine examination, the chest roentgenogram showed a cherry-sized, homogeneous, smooth-margined, well-defined, nonlobulated opacity situated anteriorly in the right upper lobe. There was no visible calcification or cavitation. The surrounding pulmonary tissue was normal. Laboratory studies and bronchoscopy showed no abnormalities. Right-sided thoracotomy revealed, anteriorly in the upper lobe and close to the surface, a round, firm nodule which was shelled out easily. Gross and microscopic examination showed a typical hamartoma. The postoperative course was uneventful.

CASE III (Fig. 3, *A* and *B*). A female, aged ten, who had previously been in good health. Three months before admission, she began to have a cough productive of blood-tinged sputum. Laboratory findings were normal; in particular, there were no signs of tuberculosis. Chest roentgenography revealed atelectasis of the apical segment of the left upper lobe. Laminagraphy disclosed one large and several smaller cavities within the infiltrated area, but no visible calcification. On left-sided thoracotomy, the apicoposterior segment of the upper lobe was found to be atelectatic, shrunken and firmly infiltrated. The area was resected and the postoperative course was uneventful. Gross and microscopic study revealed a typical hamartoma with a walnut-sized cavity lined with respiratory epithelium.

CASE IV (Fig. 4). A male, aged thirty-eight, who had been in good health up to the age of twenty. After that age, he had had repeated episodes of hemoptysis, but there had been a symptom free period of about thirteen years. During the two years preceding hospitalization, he had again developed hemoptyses and cough. Laboratory studies showed no abnormalities; specifically, no tubercle bacilli. Bronchoscopy revealed some sanguineous secretion in the branch leading to the apical segment of the right lower lobe, but no other abnormalities. Roentgenograms of the lungs showed an ill-defined infiltration, the size of the palm of a hand, at the site of the right lower lobe, but no cavitation or calcification. The same appearances were seen at laminagraphy, and bronchography showed normal conditions apart from some shrinkage of the lower lobe. Right-sided thoracotomy was performed with removal of the lower lobe, which was small and partially atelectatic. No tumors were palpable but, after the bronchial branches had been cut,

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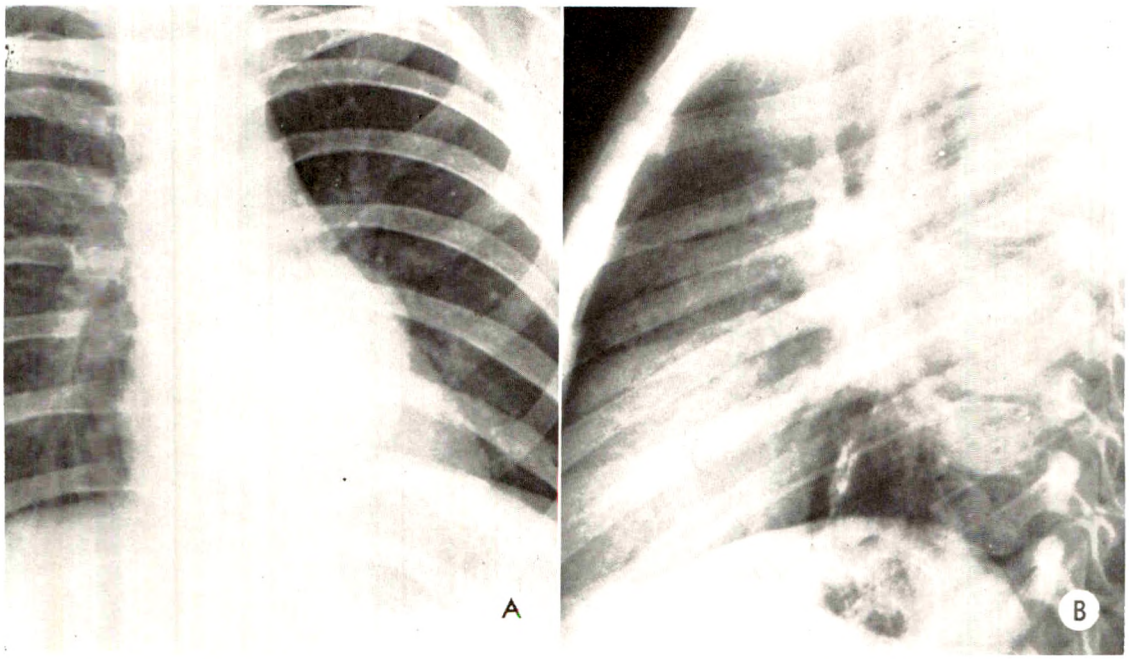


Fig. 1. Case I. (*A*) Big, round, well-defined hamartoma in the left lower lobe, visible through the heart shadow. (*B*) Lateral view.

the mucous membrane was found to be greatly thickened and vascular immediately before the branching of the bronchus to the apical segment. Histologic examination of this area revealed a typical hamartoma. The postoperative course was uneventful.

Case V (Fig. 5, *A* and *B*). A male, aged sixty-eight, who had always been in good health. Six weeks prior to admission, he started having cough and hemoptyses, but no other symptoms. Laboratory findings were normal. Bronchoscopy showed a grayish-red tumor in the bronchus to the apical segment in the right lower lobe. Roentgenograms of the lungs revealed a large, somewhat rounded, and fairly well-defined opacity beneath and behind the right hilus, at the site of the apical segment of the lower lobe. On the anteroposterior views it was partially hidden by the heart. There was no cavitation or calcification within the opacity. Bronchography showed nonfilling of the apical segment of the lower lobe, but no other abnormalities. Right-sided thoracotomy disclosed grape-like, firm, whitish masses of tumor tissue in the apical segment of the lower lobe, and the segment was resected. There was an uneventful postoperative course. Histologic examination showed a hamartoma.

Case VI (Fig. 6). A male, aged forty, with a history of right-sided pleurisy during adolescence. No other serious illnesses had been experienced; specifically, none with pulmonary symptoms. While he was in the hospital be-

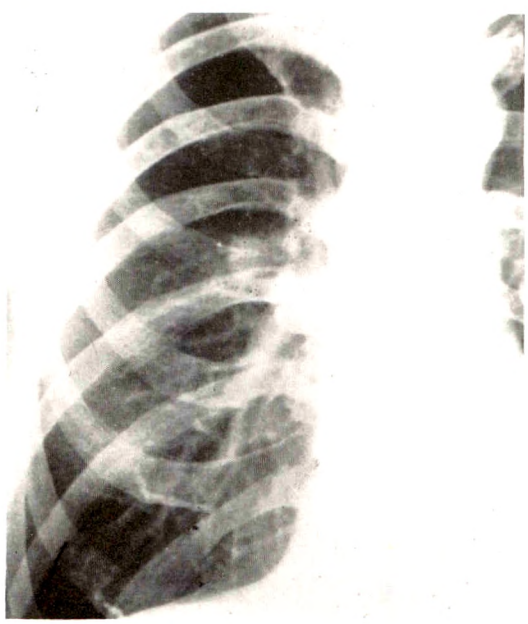


Fig. 2. Case II. Small hamartoma in the anterior segment of the right upper lobe.

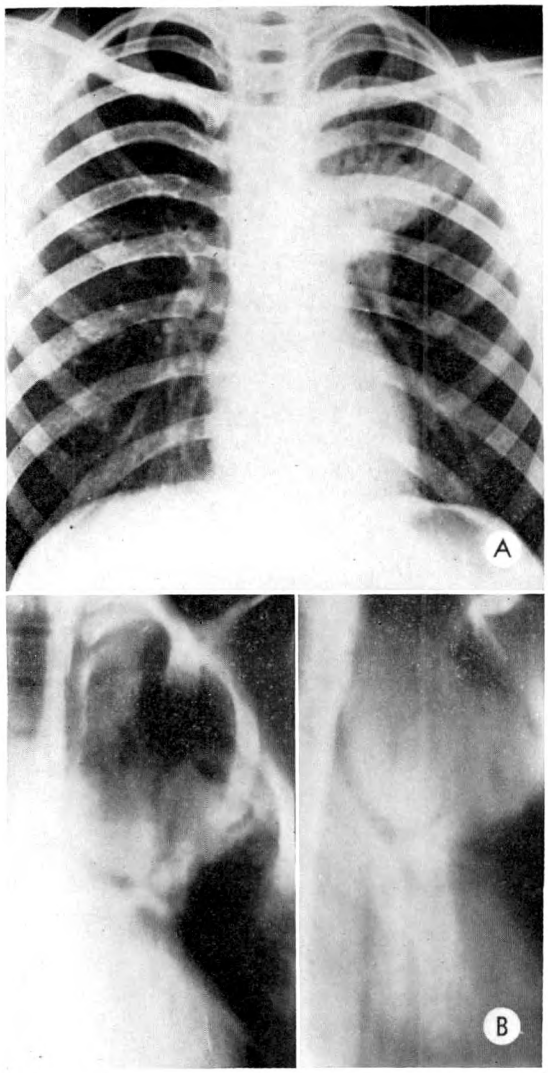


Fig. 3. Case III. (*A*) Segmental collapse of the left upper lobe due to an endobronchial hamartoma. (*B*) Laminagrams showing translucent areas within the infiltration.

cause of an injury to the knee, routine chest roentgenograms showed, apart from the sequelae of pleurisy, a walnut-sized, well-defined, rounded, homogeneous mass located peripherally in the anterior upper lobe segment on the left. Laminagrams showed no cavitation or calcifications within this opacity. Laboratory and bronchoscopic findings were normal. On left-sided thoracotomy, a firm, nodular tumor was found superficially situated in the anterior upper lobe segment and it was shelled out with ease. It was grossly as well as microscopically a typical hamartoma. There was an uneventful postoperative course.

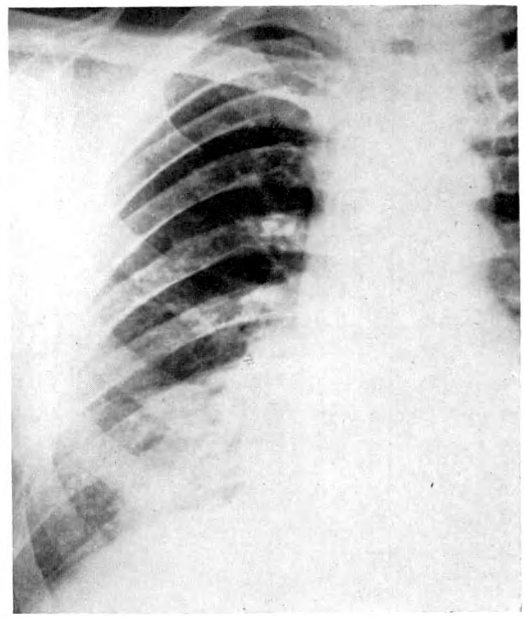


Fig. 4. Case IV. Increased density of the right lower lobe due to an endobronchial hamartoma.

Case VII (Fig. 7). A male, aged sixty-six, with a history of moderate cardiac symptoms during recent years, but no serious illnesses and no pulmonary symptoms. Routine chest roentgenograms revealed in the left lung field, behind the hilus, basally located in the upper lobe or apically in the lower lobe, a well-defined, somewhat lobular, homogeneous mass the size of a walnut. No cavitation and no calcifications were seen and the pulmonary structures in the surrounding areas were normal. There was some increase in the width of the cardiovascular shadow. Laboratory studies and bronchoscopy showed no abnormalities. Left-sided thoracotomy revealed, basally located in the upper lobe, a round, firm tumor the size of a walnut, which was shelled out easily. On gross and microscopic examination it was found to be a typical hamartoma. There was an uneventful postoperative course.

Case VIII (Fig. 8, *A* and *B*). A female, aged sixty-one with a history of supravaginal hysterectomy due to menorrhagia at the age of fifty. There had been no other serious illnesses. Owing to mild dyspeptic complaints, as an outpatient roentgen examination of the colon and stomach was done, but it showed no abnormalities. Routine roentgenograms of the lungs revealed, in the right lung field at the site of the anterobasal lower lobe segment, a

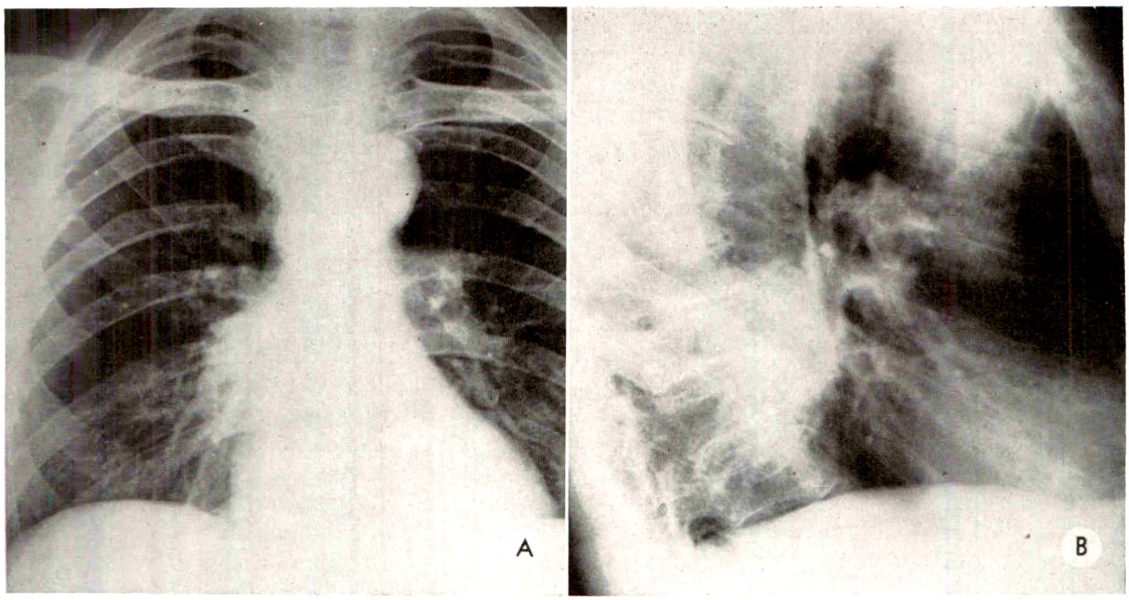


Fig. 5. Case v. (*A*) Frontal view and (*B*) lateral view showing increased density of the apical segment of the right lower lobe due to an endobronchial hamartoma.

well-defined, homogeneous, smooth-margined mass about the size of a hazel nut; surrounded by normal lung tissue. There was no visible cavitation or calcification at the site of the opacity. Laboratory findings were normal. Right-sided thoracotomy revealed in the lower lobe, just below the surface and adjacent to the middle lobe, a well-defined, firm nodule which could be shelled out easily. Gross and microscopic examination showed a typical hamartoma. There was an uneventful postoperative course.

Case ix (Fig. 9, *A* and *B*). A male, aged fifty-seven, who had always been in good

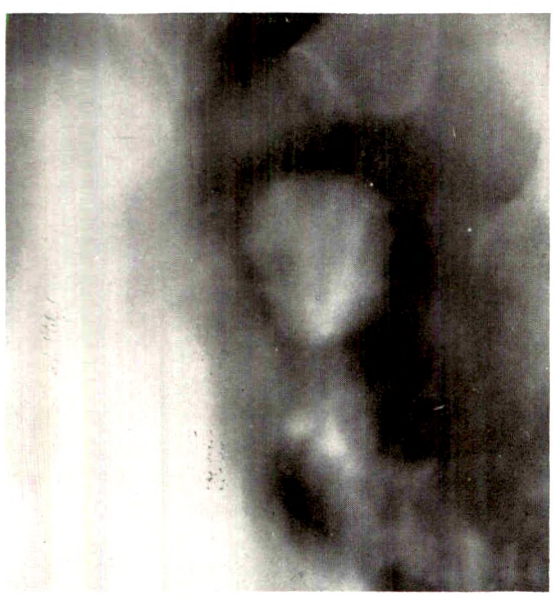


Fig. 6. Case vi. Laminagram showing a well-defined slightly lobulated hamartoma in the anterior segment of the left upper lobe.

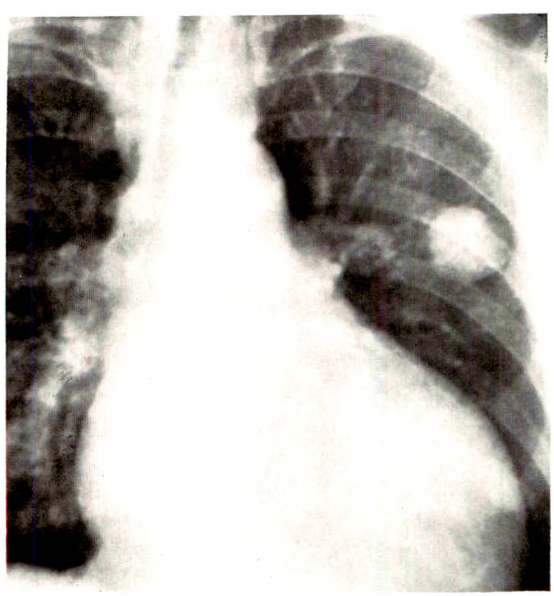


Fig. 7. Case vii. Well-defined, slightly lobulated hamartoma in the left upper lobe.

health. During the two months preceding admission, there had been moderate cough productive of sputum, which had once been blood tinged. There were no other clinical symptoms. Laboratory findings were normal; specifically, no signs of tuberculosis. Bronchoscopy showed no abnormalities. Roentgenograms of the chest demonstrated a homogeneous, well-defined, rounded, somewhat lobulated mass, the size of a hazel nut, located above the right dome of the diaphragm at the site of the middle lobe. The surrounding lung tissue was normal. Laminagraphy did not reveal any cavitation or calcification within the opacity. Right-sided thoracotomy disclosed a firm infiltration, the size of a walnut, close to the pleura. Middle lobectomy was performed and gross as well as microscopic examination revealed a typical hamartoma. The postoperative course was uneventful.

CASE X (Fig. 10, *A* and *B*). A female, aged seven, who had always had a tendency to become short of breath and to catch infectious diseases. During the six months preceding hospitalization she had had pneumonia three times. She was admitted with dyspnea and a new attack of fever. Hemoglobin was 80 per cent; erythrocyte sedimentation rate, 93 mm. Bronchoscopy showed the right main bronchus to be greatly narrowed, not admitting the bronchoscope, but no tumor tissue or foreign body was visible. Roentgen examination of the lungs demonstrated total atelectasis on the right with marked displacement of the mediastinum to the right. Centrally in the right lung around the main bronchus there was a large, irregular patch of calcification. Laminagrams did not show any necrotic cavities. On right-sided thoracotomy, the lower lobe was found to be small and atelectatic. The upper lobe was difficult to distinguish from a nodular tumor which was larger than a closed fist and which adhered to the pericardium inferoanteriorly, to the superior vena cava, and to the pulmonary artery, and was difficult to free. Lobectomy was technically out of the question, so pneumonectomy was performed. Examination of the removed specimen showed that the lower lobe bronchus was free but that it had been completely compressed by the large tumor situated in the upper lobe. The tumor was solid, grayish white, and of uniform structure with diffuse patches of calcification. Microscopic examination revealed that it was a typical hamartoma. The postoperative course was uneventful.

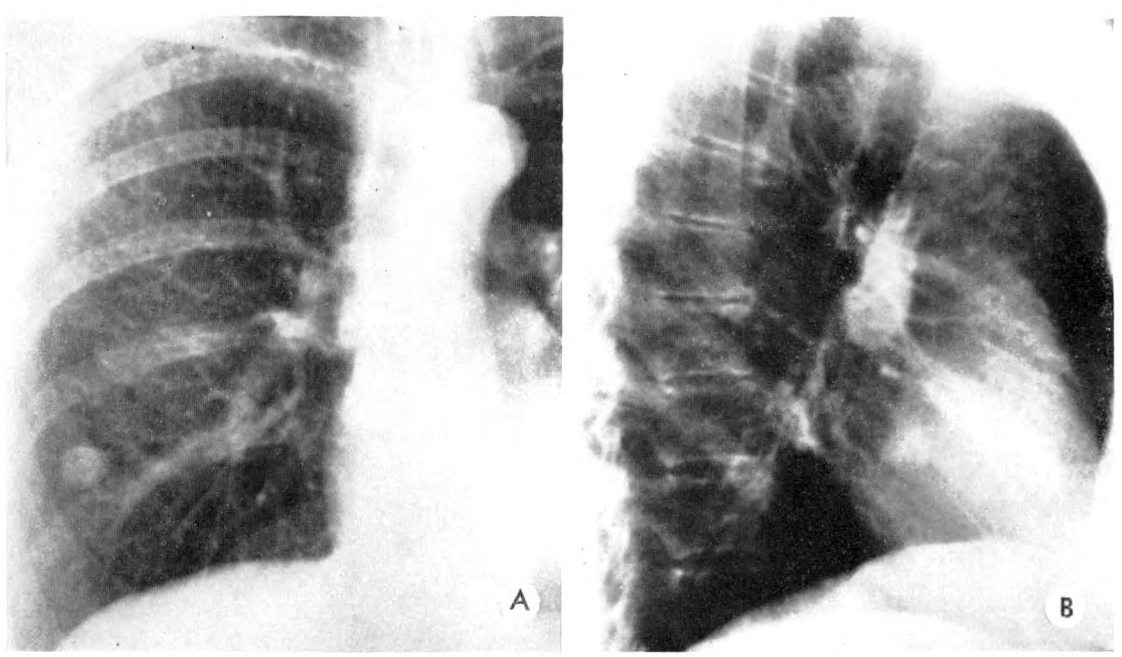


FIG. 3. Case VIII. (*A*) Small, round, well-defined hamartoma without lobulation in the anterior segment of the right lower lobe. (*B*) Lateral view.

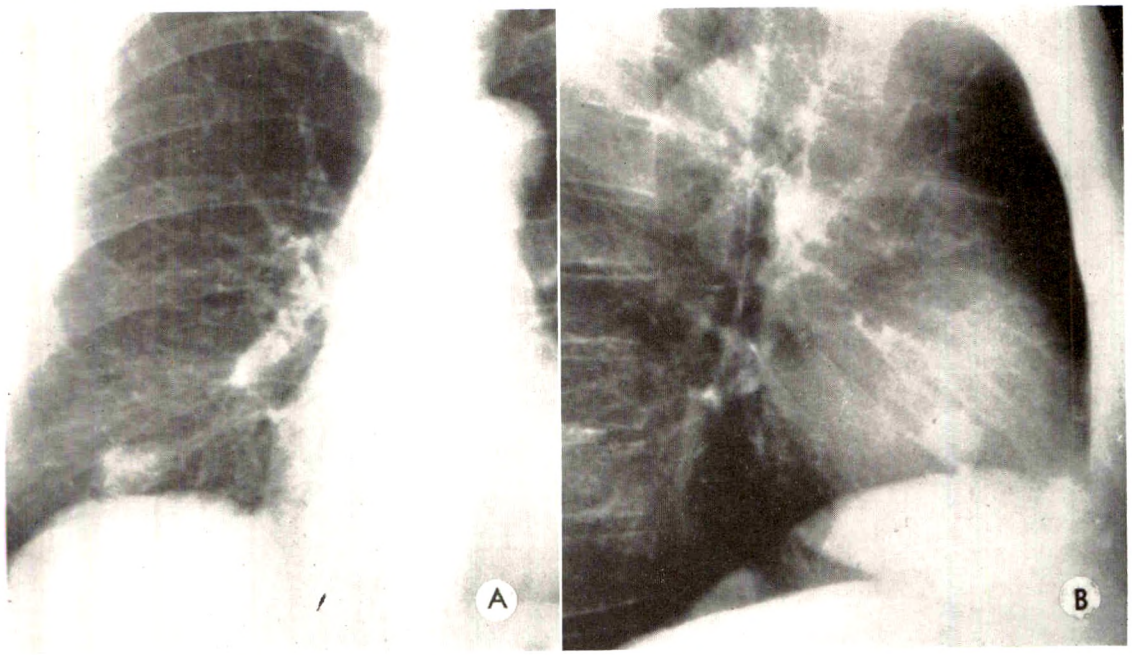


Fig. 9. Case IX. (*A*) Well-defined, lobulated hamartoma in the right middle lobe. (*B*) Lateral view.

COMMENT

Intrapulmonary Hamartomas. Cases II, VI, VII and VIII were of the intrapulmonary type. There had been no clinical symptoms or signs, and all were detected by chance. Case IX also belongs to the intrapulmonary type, but for some unknown reason the tumor had given rise to cough and hemoptysis, which led to its detection. In Case I, which likewise is of the intrapulmonary type, there had been no symptoms and the tumor was detected by chance; however, it is distinguished by its size and by the fact that the patient was only five years of age.

Endobronchial Hamartomas. The remaining four cases were of the endobronchial type. The roentgen findings in Cases III, IV and V were of segmental atelectasis due to obstruction and in Case X of unilateral total atelectasis due to obstruction as well as compression. In the last mentioned case the tumor was invasive, adhering to the pericardium and great vessels, but without any signs of malignancy. All 4 patients had clinical symptoms or signs: cough, expectoration and hemoptysis in 3, dyspnea and recurrent attacks of fever in 1 (Case X).

Only in 1 case (Case X) was calcification found in the hamartoma.

DISCUSSION

Practically all authors up to 1955 report that deposition of calcium is an important diagnostic criterion of pulmonary hamartoma. Lemon and Good[8] were the first to emphasize the uncertainty of roentgenographically demonstrating calcium within the opacity. Bleyer and Marks[2] state frankly that calcification is not of much diagnostic aid, since it is hardly demonstrable in more than about 15 per cent. Of the 15 cases of Bateson and Abbott,[1] calcifications were roentgenographically demonstrated in 2, and in the present series of 10 patients in only 1.

As regards the sex ratio, most authors report a marked male preponderance (Hickey and Simpson[6] 4:1, McDonald *et al.*[9] 3:1, and Carlsen and Kiaer[4] 3.5:1). In Lemon and Good's[8] series of 15 cases, the ratio was 2:1; while in Bleyer and Mark's[2] series and in the present report this pre-

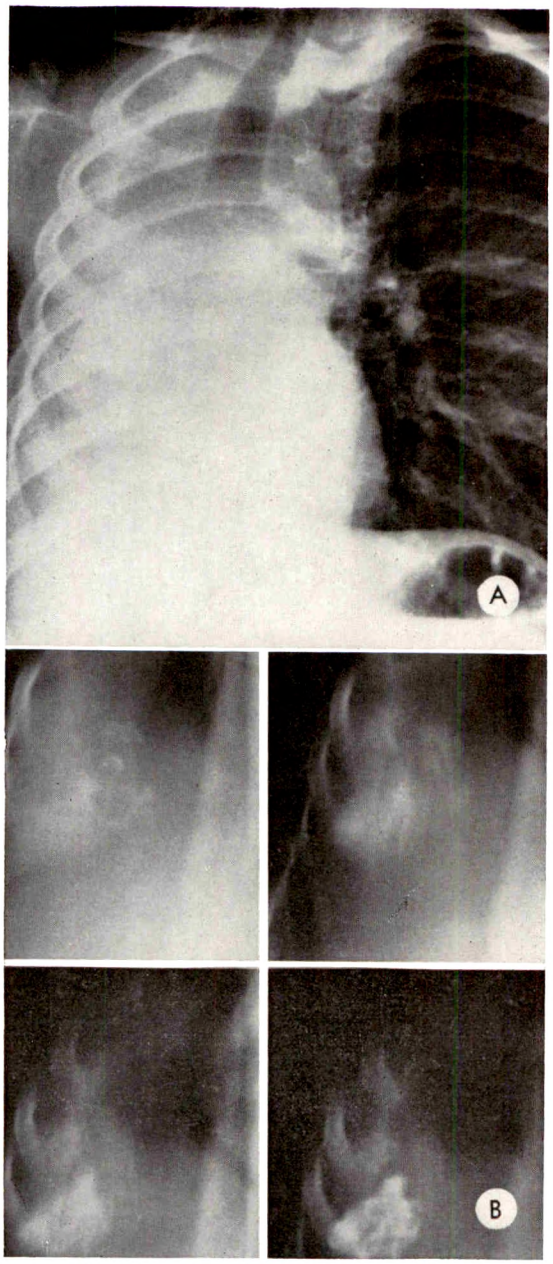


Fig. 10. Case x. (*A*) Total atelectasis of the right lung due to a hamartoma in the upper lobe. The bronchus of the upper lobe is blocked by the tumor and the bronchi of the middle and lower lobes are compressed by it. (*B*) Laminagrams showing pronounced calcifications within the tumor.

ponderance was practically nonexistent (14:11 and 6:4, respectively).

Most authors have mentioned the striking fact that a disease which, judging from all findings, is congenital is uncommon among children and adolescents. Bleyer and Marks[2] even use this fact as an aid in differentiating between tuberculoma and hamartoma, stating that only 4 per cent of hamartomas occur in patients under forty years of age. This is at variance with the present findings, 5 of 10 patients (50 per cent) being under forty and 3 of these (30 per cent) under ten years of age.

As far as the location is concerned, Bragg and Levene[3] reported the distribution to be proportional to the size of the individual lobes, the right lower lobe being most commonly involved. Lemon and Good[8] had a right-sided preponderance of 3:1. In the present series the ratio is 6:4; while Bleyer and Marks[2] had only 6 right-sided cases in 25.

Within the pulmonary tissue proper, the tumor is most often in a fairly superficial, often subpleural location. It is important to bear in mind, however, that the hamartoma may affect any part of the lung, and that a distinction must be made between the type which is remote from and the one which is close to the bronchus, *i.e.*, the intrapulmonary as opposed to the endobronchial type. The latter gives rise to bronchial irritation leading to cough and expectoration and in some cases hemoptysis (Cases III, IV and V). Roentgenologically, the appearance is characterized by atelectasis at the site of the involved area. In the more unusual cases of pronounced obstruction, the clinical signs are dyspnea and recurrent pneumonia (Case X).

The intrapulmonary type is more common, presenting roentgenologically as a roundish, smooth-margined, well-defined, and frequently somewhat lobulated mass (coin lesion) with normal surrounding lung tissue. It seldom gives rise to symptoms, but according to the literature it may at times cause pain, possibly due to pressure upon intercostal nerves (Bateson and Abbott[1]).

In the present series 6 were intrapulmonary. Only 1 of these patients (Case IX)

had clinical symptoms, which were in the form of bronchial irritation causing cough and hemoptysis on one occasion. The explanation is not known.

According to Bateson and Abbott,[1] in a review of the 253 published cases of pulmonary hamartoma, 226 belonged to the intrapulmonary and only 27 to the endobronchial type. This report adds 10 cases, 6 of them intrapulmonary and 4 endobronchial.

SUMMARY

Ten new cases of pulmonary hamartoma are reported. Six were of the more common intrapulmonary type showing the usual roentgen appearance (coin lesion), and only 1 of these 6 patients had clinical symptoms of pulmonary disease. The remaining 4 cases belonged to the very rare endobronchial type, which has been reported previously in only 27 instances. This type is characterized roentgenologically by obstruction atelectasis and gives rise to clinical symptoms and signs, *viz*, cough, expectoration and, in some cases, hemoptysis and recurrent pneumonia. Five of the patients were under forty years of age, 3 of them being under ten years of age.

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CYSTITIS EMPHYSEMATOSA*

19 CASES WITH INTRALUMINAL AND INTERSTITIAL COLLECTIONS OF GAS

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THE presence of gas in the urinary bladder, although stated to be a rare condition, has been the subject of numerous reports in the medical literature.

Cystitis emphysematosa, the presence of gas vesicles in the wall of the bladder, has been arbitrarily distinguished from primary pneumaturia, the presence of gas in the lumen of the bladder, with or without its passage via the urethra. There appears to be no justification for this distinction since they would appear to be different and occasionally concomitant stages of the same basic disease process with common etiologic factors. Despite this, separate and exclusive literatures have developed under each heading, and the essential identity of the two conditions has not been stressed.

PRIMARY PNEUMATURIA

The literature on primary pneumaturia is considerably more voluminous than that on cystitis emphysematosa and dates back to 1671, when, in a publication entitled "Curiosities of Nature" a case was described in which gas was found in the urinary bladder.[28] In 1825 Boismont made reference to spontaneous formation of gas in the bladder,[8] and in 1882 Keyes[12] reported the first 2 cases in the American literature, although these were apparently the result of instrumentation. Senator[25] was the first to propose a classification of causes of gas in the bladder in 1891. He divided cases into three groups: (1) those due to instrumentation, (2) those due to the presence of fistulous connections between the bladder and the bowel, and (3) spontaneous formation of gas in the bladder. In this latter group are the cases with which we are dealing when we speak about "primary" pneumaturia and cystitis emphysematosa, although it is not always possible to distinguish with certainty between group 1 and group 3. In 1898 Kelly and MacCallum[10] reviewed the literature and were able to find 16 cases of gas in the bladder due to fermentation. Nine of the 16 had glycosuria and several of the cases had an associated obstruction of the lower urinary tract. There were no bacteriologic studies of these early cases. Mulsow and Gillies[23] are credited with the first report of a patient in whom the diagnosis of pneumaturia was made roentgenographically.

Between 1898 and 1948 there were many isolated case reports, the majority being in the German literature. In 1948 Arthur and Johnson[1] reported a case in a diabetic female in which *E. coli* was the organism incriminated as the cause of the underlying cystitis. They were able to find 25 cases in the literature with their own being the 26th. Of these only 5 were found in the American literature. Spring and Hymes[27] again reviewed the literature in 1952 and were able to find 38 cases, with glycosuria being present in 21 of these. They tabulated the glycosuric and nonglycosuric cases and showed that the responsible organism in the majority was either *E. coli* or *Aerobacter aerogenes* with inconstant findings of other organisms, including *B. proteus*, *Staph. aureus*, *Streptococci*, *Nocardia*, yeasts and in one case *B. Friedländer*. (It is worthy of note that *Aerobacter aerogenes* and *B. Friedländer* are bacteriologically indistinguishable and are only recognized as different entities by the different pathologic conditions which they produce. It would seem highly likely that the infecting organism in the case cited was, as in many of the re-

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maining reports, *Aerobacter aerogenes* also.) They were likewise able to find a high incidence of urinary retention due to a variety of causes including benign prostatic hypertrophy, cord bladder, and diverticula of the bladder. There was invariably an associated infection. Since that time several other cases have been reported.[2,7,8,17,30] All of these cases were diabetic patients. A further case has been noted by Kent[11] who reported in addition, 3 cases with gas in the urinary bladder, apparently due to fistulous connections between the bladder and the gastrointestinal tract.

Fineman *et al.*[7] were able to find only 4 references to the roentgenologic diagnosis of primary pneumaturia. Boijsen and Lewis-Jonsson[2] were the first authors to hint at the identity of primary pneumaturia and cystitis emphysematosa. Their paper contains references to the literature under both headings and the roentgenograms reproduced in their paper clearly show, as do roentgenograms reproduced in other papers on cystitis emphysematosa, the presence of gas both in the lumen of the bladder and within the bladder wall. Thomas and Sandler,[30] in reporting their case, state that cystitis emphysematosa occurs only rarely with pneumaturia.

CYSTITIS EMPHYSEMATOSA

The condition "cystitis emphysematosa" was originally described as a pathologic entity only. Hueper,[9] in 1926, described the changes of cystitis emphysematosa in a female dog which was submitted to him for autopsy. The dog proved to have glycosuria, hyperglycemia and changes in the pancreas which included complete absence of islets of Langerhans. No bacteriologic studies were made. He described an additional 11 clinical cases collected from the literature, but there are few clinical data on these cases and there were apparently no adequate urinary studies. To Mills[18–21] goes the credit for giving excellent pathologic descriptions in a series of 12 cases reported in 1930. These were all seen at autopsy. Originally, he was uncertain as to whether the findings represented postmortem changes or results of disease in the living subject. However, he eventually came to the conclusion that the disease was a clinical entity and that it would ultimately be demonstrated in a living subject. None of Mills' patients were diabetics, but he pointed out that 2 of his subjects had had repeated intravenous glucose infusions. The presence of glycosuria in these 2 patients was not stated. His predictions regarding the discovery of cystitis emphysematosa in a living subject were shortly confirmed by Ravich and Katzen,[24] who reported a case in a living patient with recovery. Following this, several observers noted the condition on cystoscopic examination of the bladder. Burrell[4] gave a description of the cystoscopic appearances in a nondiabetic and was able to reproduce the condition by means of an ingenious experiment. He produced a chemical cystitis by means of silver nitrate in a male rabbit made glycosuric by the intravenous infusion of glucose and then inoculated the bladder with the responsible organism (*E. coli*) from a patient having cystitis emphysematosa. The rabbit developed the typical changes in the bladder wall. Other descriptions of cystoscopic findings were given by Levin,[14] Lund *et al.*,[15] Marquardt,[16] and Burns.[3] Lund *et al.* were able to collect gas from the vesicles and found it to be carbon dioxide.

Wells,[31,32] in 1938, reported 7 cases of cystitis emphysematosa. Only one case had glycosuria and he stated that he could find that neither glycosuria nor trauma were significant etiologic factors. He also described the pathologic findings in a subsequent paper. In 1949, Teasley[29] reviewed the 43 cases in the literature and added one case of his own, a diabetic patient. Seven of these were in diabetics. He cited infection with *E. coli* and hyperglycemia as common findings (although sufficient bacteriologic and urinary data were not available on many of the earlier cases, as previously noted). Since that time cases have been reported by Milner *et al.*,[22] Faingold *et al.*,[6] Zatzkin,[33] Lane and Francke,[13] and Sotero-

poulos *et al.*[26] Faingold and co-workers'[6] 4 cases all showed glycosuria, 2 of them being confirmed diabetics, the remaining 2 having glycosuria at some time during the course of their illness but with diabetes not definitely established. Three of these had *E. coli* as the infecting organism and the diagnosis was made roentgenologically in all 4 cases. They pointed out that the condition was transitory in nature and offered this as an explanation for its apparent rarity as a diagnosis. Zatzkin's[33] case was in a patient who had glycosuria associated with hemochromatosis. The infecting organism was not stated. The case of Soteropoulos *et al.*[26] was in a diabetic and is of interest as being the first reported case in which the vesicles were seen to extend into the distal third of both ureters. They cultured *E. coli* and *Aerobacter aerogenes* from the urine.

In all, there appear to be 52 cases in the literature under the heading of "cystitis emphysematosa." Of these, 13 were known to have glycosuria. Data in some of the remainder are incomplete. *E. coli* is the common denominator from a bacteriologic standpoint. Under the heading "primary pneumaturia," there appear to be 46 other cases in the literature, 29 of which had glycosuria. We are reporting an additional group of 19 cases (Table I and II).

The increasing frequency of diagnosis is apparently due to the increasing awareness of clinicians and radiologists of this condition.

It is the impression of the author that the literature on each subject should now be integrated. Findings common to the two conditions as seen in the many reported cases include (1) high incidence of glycosuria in the presence of urinary stasis and obstruction, (2) infection with *E. coli* or *Aerobacter aerogenes*, and (3) production of gas in the wall of the bladder, in the bladder lumen, or in both places.

CASE MATERIAL

During the twelve year period from 1949 through 1960, 19 patients have been studied in the radiology department of the New England Deaconess Hospital with evidence of gas either in the wall or the lumen of the urinary bladder or in both places. Fifteen of these cases have been seen in the last three years.

The 19 cases comprise 15 diabetic and 4 nondiabetic patients. Five of the 6 male patients and 10 of the 13 female patients suffered from diabetes. In 3 cases, 1 male and 2 female, episodes of cystitis emphysematosa occurred on two separate occasions with evidence of persisting urinary tract infections in the intervening period.

ILLUSTRATIVE CASE HISTORIES

CASE 3. B.S. This twenty-five year old white female was admitted to the New England Deaconess Hospital for the twelfth time on October 22, 1958, her previous admissions being connected with the complications and control of her diabetes which had been diagnosed fifteen years previously. She had been fairly well until the day of admission when she experienced gross hematuria and crampy pain in the left flank radiating into the left groin. She vomited repeatedly.

Physical examination: Well developed and well nourished. Pulse 76, temperature 99° F.; heart and lungs were normal. The popliteal pulses were not palpable. There was marked tenderness in the left costovertebral angle and also in the left lower quadrant.

Urinalysis: Grossly bloody specimen, albumin 65 mg. per cent, glucose 2.5 gm. per cent and there were 80 to 100 white blood cells per high power field. The nonprotein nitrogen was 55 mg. per cent. Urine culture showed *Aerobacter aerogenes.*

An admission roentgenogram of the abdomen showed gas in the lumen and in the wall of the bladder. An intravenous pyelogram revealed evidence of right sided chronic pyelonephritis and a questionable cyst on the left kidney together with an estimated 6 ounces of residual urine.

Course: She was treated with achromycin, sedatives and analgesics and her diabetes was brought under control. On this regimen her symptoms subsided and she was discharged on November 4, 1958. She was again admitted with a urinary tract infection and gross hematuria on November 4, 1959. On this admission a retrograde pyelogram revealed filling defects in

TABLE I

PERTINENT FINDINGS IN CASES STUDIED

Case No.	Age and Sex	Diabetes (yr.)	Associated Conditions	Organism	Urine Data Reaction	Urine Data Glucose	Red Blood Cells	White Blood Cells	Remarks
1 A.B.	65F	10	Diabetic neuropathy; horseshoe kidney; arteriosclerotic hypertensive heart disease	*E. coli*	acid	o-tr.	o	60–80	Minimal glycosuria
2. M.B.	72F	—	Cystocele; bedridden 20 yr.; Menière's disease 20 yr.; frequency and spasmodic incontinence many years	*Staph. aureus*	acid	o	10–20	10–20	On catheter drainage of bladder low bladder capacity of 180–200 cc.
3 B.S.	25F	15	Retinopathy; nephropathy; neuropathy; degenerative vascular disease; chronic pyelonephritis	*Aerobacter aerogenes;* *B. proteus*	1. acid 2. acid	+ +	gross o	80–100	Two separate episodes of cystitis emphysematosa
4 M.M.	44F	—	Bilateral narrowing of renal arteries on aortogram; small right kidney	—	alkaline	o	o	o	Catheterized two weeks prior to intravenous pyelography; no cystoscopy; had splenorenal shunt operation for narrowing of left renal artery
5 E.F.	36F	14	Diabetic nephropathy and retinopathy	*E. coli*	acid	o	o	25–45	"Tests very good" for few days prior to admission
6 C.N.	26F	14	Diabetic neuropathy; nephropathy and retinopathy with residual urine of 400 cc.	*E. coli*, *Aerobactor aerogenes*	alkaline	+	gross	—	Volunteered that she had passed gas in urine; had had poor diabetic control with frequent high blood sugar readings
7 A.O.	77F	35	Pernicious anemia 12 yr.; aortic stenosis	*E. coli*	acid	+	gross	100–125	Gas observed during fluoroscopy for gastrointestinal series; died during a subsequent admission with *E. coli* septicemia
8 M.D.	64F	22	Chronic urinary infection; diabetic retinopathy	*E. coli*	acid	+	gross	??	Passed gas in urine on 2 or 3 occasions; much residual urine; *E. coli* isolated was a marked gas producer; readmitted 2 yr. later with gas in bladder
9 A.R.	55F	—	Urinary tract infection 37 yr.	*E. coli*	alkaline	o	o	—	Retrograde pyelography 7 da. previously; bladder obscured by rectal contents at that time
10 A.K.	80M	13	Diabetic neuropathy; cardiac decompensation	*E. coli*	acid	o	o	40–60	Little or no glycosuria on admission in spite of a blood sugar of 275; died from cerebrovascular accident; no autopsy or urine data on last admission
11 A.S.	61F	2	Cardiac decompensation led to admission; hematuria developed after admission; diabetic neuropathy	*E. coli*, *Strep. anhemolyticus*	?	?	gross	?	Fairly large residual urine of 250 cc.; cystitis emphysematosa cleared in 4 days
12 J.B.	61M	8 mo.	Large prostate; prostatectomy; postoperative pneumonia	*Aerobacter aerogenes*	acid	+	gross	10–20	Trabeculation and stasis in bladder probably on basis of prostatic enlargement; prostatectomy with postoperative pneumonia; agranulocytosis; autopsy
13 M.M.	67F	13	Hypertension; diabetic neuropathy	*E. coli*	acid	+	o	80–100	
14 C.T.	83M	—	Gastric ulcer treated surgically; colonic and bladder diverticula	*E. coli;* *Aerobacter aerogenes;* *Staph. aureus*	alkaline	o	occasional	250–75	Gastrointestinal studies showed gas probably in diverticulum prior to cystoscopy; definite gas in diverticulum after cystoscopy; no evidence of fistulae on cystoscopic examination
15 E.L.	54F	23	Arteriosclerotic heart disease; neuropathy; hiatus hernia; "nephrotic syndrome"; 24 previous admissions	*Aerobacter aerogenes*	alkaline	o	occasional	150–175	Persistent *E. coli* urinary tract infections on subsequent admissions
16 C.B.	61M	6	Neuropathy; previous transurethral resection	*E. coli;* *B. proteus*	?	o-tr.	gross	??	Occasionally passed gas in urine over 2 yr. period but this fact had to be elicited by direct questioning
17 B.D.	23M	10	Diabetic retinopathy; neuropathy; nephropathy	*Aerobacter aerogenes*	acid	+	occasional	100–125	Gas demonstrated in bladder at outside hospital 1 yr. previously
18 F.H.	53M	26	Old tuberculosis treated by surgery; neuropathy; ?retinopathy	*Aerobacter aerogenes*	acid	+	occasional	30–45	Persistence of gas for 1 wk. associated with persistent *Aerobacter aerogenes* in urine; gas disappeared after 14 da.; urine sterile
19 K.B.	27F	12	Bilateral cataracts; bladder neuropathy; severe degenerative vascular disease	*E. coli*	alkaline	+	occasional	30–40	Calcified pelvic vessels; seen 2 yr. later; no gas present in urinary tract

TABLE II

ROENTGEN FINDINGS IN 19 CASES WITH GAS IN THE BLADDER

Case No.	Diagnosis of Gas: Clinical	Diagnosis of Gas: Roentgenologic	Time to Clear	Manifestation: Intramural	Manifestation: Intraluminal
1	o	+	Less than 5 da.	+	+
2	o	+		−	+
3	o	+		+	+
	o	+		±	+
4	o	+		−	+
5	o	+		+	−
6	+	+		+	+
7	o	+		±	+
8	+	+	4 da.	−	+
9	o	+		+	+
10	+	+	4 da.	+	+
11	o	+		+	+
12	o	+	Less than 2 wk.	+	−
13	o	+		−	+
14	o	+		−	+
15	o	+		−	+
16	o	+		±	+
17	+	+	4 da.	+	+
18	o	+		+	+
19	o	+	4 to 5 da.	+	+

the renal pelves (? blood clot) but no evidence of gas in the bladder. She was treated with bed rest, antibiotics and control of her diabetes. The symptoms again subsided. A culture of the urine at this time again revealed *Aerobacter aerogenes*.

On her fourteenth admission on January 25, 1960, she complained of chills and fever, which had been attributed to an upper respiratory tract infection. Physical examination was essentially negative except for blood pressure of 160/110 and pulse of 104. Diabetic retinopathy was noted. On January 27, a roentgenogram of the abdomen showed air-fluid levels in the bladder together with a slight degree of intestinal ileus. An intravenous pyelogram four days later showed evidence of bilateral pyelonephritis in the form of slightly dilated calyces. Bubbles of gas were seen in the bladder and there was residual urine of approximately 6 ounces. Urine culture revealed *B. proteus*. She was treated with insulin, bed rest and chloromycetin, whereupon her symptoms subsided and she was discharged improved on February 3.

Comment. A typical case of primary cystitis emphysematosa with evidence of gas both in the lumen and in the wall of the bladder in the presence of diabetes and stasis, due, in this case, to diabetic neuropathy. Infection of the urine with *Aerobacter aerogenes* was demonstrated on several occasions. It seems possible that the *B. proteus* organism cultured on the last admission may have masked the presence of an infection with another gas-forming organism. It is of interest that the condition recurred after treament and on each occasion responded without undue local sequelae.

CASE 7. A.O. This seventy-seven year old white female diabetic of thirty-five years' duration was admitted to the New England Deaconess Hospital for the twelfth time on June 20, 1958. She had been under treatment for the past twelve years for pernicious anemia in addition to her diabetes mellitus.

She complained of dysuria which had been of fairly recent onset and she had noted gross blood in her urine which was also cloudy. Previous admissions had been in connection with her diabetic control and treatment of her anemia. On one occasion there had been noted a high blood sugar in the absence of glycosuria and on a further occasion bacteruria had been observed.

Physical examination: Not remarkable except for a Grade IV systolic murmur at the apex. Blood pressure was normal and the lungs were clear.

Urinalysis: Specific gravity of 1.005, acid reaction, albumin 19 mg. per cent, glucose 0.3 gm. per cent and 80 to 120 white blood cells per high power field. Cultures of the urine revealed *E. coli*. On the eighth hospital day, gas was observed in the bladder during examination of the gastrointestinal tract. This was confirmed on an intravenous pyelogram two days later which showed good function of each kidney, an air-fluid level in the bladder and a residual urine of greater than 6 ounces.

Course: The patient was treated with chloromycetin and insulin on which regimen she showed marked improvement and was discharged on July 1, 1958. She was re-admitted on December 11, 1958 complaining of "weakness" for two days prior to admission. Thirty-six hours prior to admission she had vomited bile-stained material and twelve hours after this had experienced the onset of generalized

upper abdominal pain with diarrhea. This had continued up until the time of her admission.

Physical examination on this occasion revealed a blood pressure of 60/40 with pulse of 100 per minute and temperature of 99 degrees. The remainder of the examination was unremarkable except for the previously noted cardiac murmur and slight left upper quadrant tenderness.

Laboratory findings: Hemoglobin 11.9 gm. per cent, white blood cells 24,700 rising later to 70,700 with 34 per cent band forms. Serum electrolytes were normal. Blood sugar was 294 mg. per cent. A blood culture disclosed *E. coli* as did a culture of the urine. Urinalysis revealed 200 mg. per cent of albumin, 40 red blood cells per high power field and 10 to 12 white blood cells per high power field. She was treated with intravenous fluids and sympathomimetic amines, but she developed pulmonary edema and died approximately twelve hours after admission.

Autopsy findings: Cultures of the heart blood, spleen and kidney grew *E. coli*. The kidneys showed scattered yellow nodules in both the cortex and the medulla, the nature of which was not clear. There was no evidence of diabetic nephropathy. The bladder wall was thickened, measuring up to 0.8 cm., with a somewhat firm, polypoid mottled red surface. Microscopically, the bladder showed submucosal infiltration with chronic inflammatory cells, dilatation of blood vessels and occasional hemorrhages.

Comment. This patient is of interest because she had shown on one occasion discrepancy between the blood sugar and the urine sugar, a feature of cystitis emphysematosa which has been mentioned by previous authors.[27] Stasis was also present, presumably on the basis of diabetic neuropathy. She subsequently succumbed to a septicemia with the same organism which was responsible for her bladder infection.

Case 8. M.D. This sixty-four year old white female was admitted to the New England Deaconess Hospital for the first time in January of 1958 with a urinary tract infection (*Aerobacter aerogenes*) which was successfully treated with penicillin and streptomycin. She was discharged, but was re-admitted in July, 1958 with gangrene of the toes of the right foot for which a transmetatarsal amputation was performed. At the time of her admission on November 19, 1958 she had had diabetes mellitus for a total of twenty-two years. She complained at this time of intermittent painless hematuria of six days' duration with passage of gas in the urine on two or three occasions. There was frequency of urination, every two to three hours by day and two to three times during the night.

Physical examination: Well nourished woman, not in great distress. The temperature was 99° F., pulse 90, and blood pressure was 135/60. Heart and lungs were negative. Abdominal examination gave the sensation of a suprapubic mass. Ankle jerks were absent. Diabetic retinopathy was noted.

Urinalysis: Specific gravity 1.010, acid reaction, albumin 470 mg. per cent, glucose 2.2 gm. per cent, and the specimen was "loaded" with red blood cells. Culture of the urine revealed a strain of *E. coli* which produced considerably more gas than a strain of *E. coli* selected at random from those under culture in the laboratory, both growing in a glucose medium. On the second hospital day, an intravenous pyelogram disclosed gas in the bladder lumen which persisted after voiding.

Course: The patient was treated with achromycin and insulin under which regimen her symptoms subsided. However, she was readmitted one year later at which time she again had an *E. coli* urinary tract infection, but with no evidence of gas in the bladder. A further re-admission in November, 1960 showed the bladder to be distended with gas almost to the level of the umbilicus and an infection with *E. coli*. This was again treated with antibiotics. A roentgenogram of the abdomen one month later showed it to be distended but with no gas present.

Comment. This is the only case in the series in which the propensity of the infecting organism for gas production was tested. It might well be that others, if tested, would have shown this property.

Case 12. J.B. This sixty-one year old white male was admitted to the New England Deaconess Hospital for the first time on December 13, 1957 with a six to eight month history of polydypsia and polyuria. Glycosuria and acetonuria had been discovered four days prior to admission. Eight hours prior to admission he began to void blood-stained urine. The past history was essentially negative. Physical examination: Male in acute distress with marked urgency of urination. Heart and lungs were

normal. There was diffuse suprapubic tenderness. The prostate gland was enlarged. The remainder of the examination was essentially negative.

Urinalysis: Specific gravity 1.015, acid reaction, albumin 152 mg. per cent, glucose 1.3 gm. per cent, 70 to 90 red blood cells per high power field, 19 to 20 white blood cells per high power field and bacteria 4 plus. Culture of the urine on two occasions revealed *Aerobacter aerogenes*. The hemoglobin was 13.4 gm. per cent, white blood cells 12,900 with a shift to the left. Blood sugar was 94 on admission and 214 on the second hospital day. On the third hospital day, an intravenous pyelogram revealed trabeculation of the bladder dome with questionable gas vesicles within the wall of the bladder. Re-examination of the pelvis after careful preparation of the rectum on the following day showed positive evidence of gas bubbles in the wall of the bladder.

Course: The diabetes was controlled on 35 units NPH insulin. On the sixth hospital day a cystoscopy revealed a bladder of limited capacity with multiple ecchymotic areas on the posterior wall. At the junction of the floor and posterior wall, there were hyperemic rugations with tiny, gray cysts. A biopsy of the bladder wall was reported as showing chronic inflammation and fibrosis. Subsequently, he developed a postoperative pneumonia and both this and his urinary tract infection proved refractory to all antibiotics which included chloromycetin, gantrisin, achromycin, polymyxin, furadantin, streptomycin, triple sulfa and albamycin. Following this he developed agranulocytosis and succumbed to a septicemia on February 9, 1958. An autopsy showed an organizing pneumonia of the right middle lobe with terminal aspiration and pulmonary edema. A swab from the prostate gland showed *E. coli* and a swab from the bladder revealed *Pseudomonas* and *Streptococcus hemolyticus*. Examination of the bladder showed it to be markedly hemorrhagic with papillary projections around the area of entrance of the indwelling catheter. In addition, this area was markedly friable. On the posterior wall just above the trigone, there was an almost perfectly round area of denudation of the mucosa with surrounding radial puckering of the wall. The whole of the bladder had a "boggy" consistency. The prostate gland showed many thick walled abscesses up to 1.5 cm. in diameter. Multiple venous thromboses were present. Microscopic examination of the bladder showed acute and chronic inflammatory cells. There were nests of normal mucosal cells below the level of the rest of the mucosa plus a fibrous, healing ulcer. A necrotic area containing clumps of bacteria was situated near the bladder dome and was surrounded by congested vessels, occasional hemorrhages, and a zone of reaction composed mostly of eosinophils, lymphocytes and monocytes.

Comment. This is a case of cystitis emphysematosa with cystoscopic findings. Persistent infections in the bladder region and a complicating postoperative pneumonia with the exhibition of multiple antibiotics in an attempt to control these infections apparently resulted in agranulocytosis and death from septicemia. Autopsy also showed severe prostatic infection, but it is not clear whether the prostatic infection preceded the bladder infection or vice versa. The cystoscopic appearance corresponds fairly closely with that previously noted by Mills[18–21] and others.

FINDINGS

The pertinent clinical, roentgenologic and laboratory data of the 19 cases studied are summarized in Tables I and II. There was a striking preponderance of females to males in an approximate ratio of two to one.

The age of the patients ranged from twenty-three to eighty-three years. Of the 15 diabetic patients, the average duration of diabetes was 14.2 years with a range of a "few months" to 35 years. The salient clinical findings were a high incidence of glycosuria and evidence of urinary tract infection, which was often recurrent. Gross hematuria was a common finding in cases in which gas in the bladder wall was a feature. Subsequent histologic examination in 2 such cases showed hemorrhage within the bladder wall. The responsible organism in almost every instance was either *E. coli* or *Aerobacter aerogenes*, the two exceptions being Case 3 and 4. In the former case the organism cultured during one of her two episodes of cystitis emphysematosa was

B. proteus, an organism noted for tending to "swarm" over other organisms growing with it. In the other case the culture of the urine showed "no growth." This patient had, however, been on antibiotic therapy shortly before the diagnosis was established.

Diagnosis was made by roentgen examination alone in 15 cases and by both roentgenograms and clinical history in the remaining 4 cases. Gas in the wall of the bladder was the sole manifestation in 2 cases; gas in the lumen of the bladder was the most prominent feature in a further 6 cases, and the remaining 11 cases had evidence of gas in both the wall and the lumen of the bladder. Only 2 of the patients who had gas present in the lumen of the bladder volunteered the information that they had passed gas when voiding. One further patient gave this information on direct questioning after gas was discovered by roentgen examination.

It is to be noted that 4 of the diabetic patients had negative tests for urine glucose on admission.

Associated findings included a high proportion of chronic urinary tract infections and urinary stasis. Stasis in the diabetic patients was evidently due chiefly to bladder neuropathy. In the 6 cases of which follow-up roentgenograms were available, the time taken for the gas to disappear under treatment was less than four days in 4 cases, and an indeterminate period less than two weeks in another case. Persistence of gas in the remaining case was associated with persistence of the infecting organism in the urine despite the antibiotic treatment and control of diabetes. The urine was acid in reaction in 10 cases, alkaline in 4 (including 3 of the 4 nondiabetic patients) and in a further case this information is not present in the laboratory data.

Of the 2 cases which came to autopsy, the findings in the bladder were those of an acute and chronic submucosal inflammatory reaction. One of the cases was also cystoscoped prior to death and the bladder showed an intense hemorrhagic reaction with vesicles and ulcerated areas in the mucosa.

ROENTGEN FEATURES

The gas within the bladder wall or lumen, which is the essential feature of this condition, must be distinguished from gas in the rectum and sigmoid. This is usually not difficult, but, if necessary, roentgenograms of the bladder region with the patient in the erect position must be taken to demonstrate the characteristic air-fluid level (Fig. 3, *A* and *B*). The gas is usually visible on plain roentgenograms taken in the supine or erect position. An intravenous pyelogram is not essential in order to make the diagnosis but gives valuable additional information regarding contributory factors (Fig. 4, *A* and *B*). It may show prostatic hyperplasia with obstruction or a large residue resulting from diabetic neuropathy.

When the gas is situated chiefly in the wall of the bladder, diagnosis presents no difficulty since the appearance is quite characteristic. It consists of a narrow radiolucent line of gas bubbles outlining the bladder wall when seen in profile and a collection of vesicles varying in size from a few millimeters up to one centimeter and having a "cobble-stone" appearance when seen "*en face*." In most of these latter cases a collection of intraluminal gas is also present (Fig. 1, *A* and *B*). Persistence of gas after a few days of treatment is invariably associated with persistence of the infection.

In those cases where intraluminal gas is the predominant feature, careful inspection will usually reveal the presence of a few bubbles within the tissues of the bladder wall (Fig. 2, *A* and *B*).

DISCUSSION

It would appear that cystitis emphysematosa is a condition which is not so rare as many previous reports would indicate. Experience in this department of radiology would seem to suggest that it is increasing in frequency since we have seen 15 cases in the last three years as compared to only 4

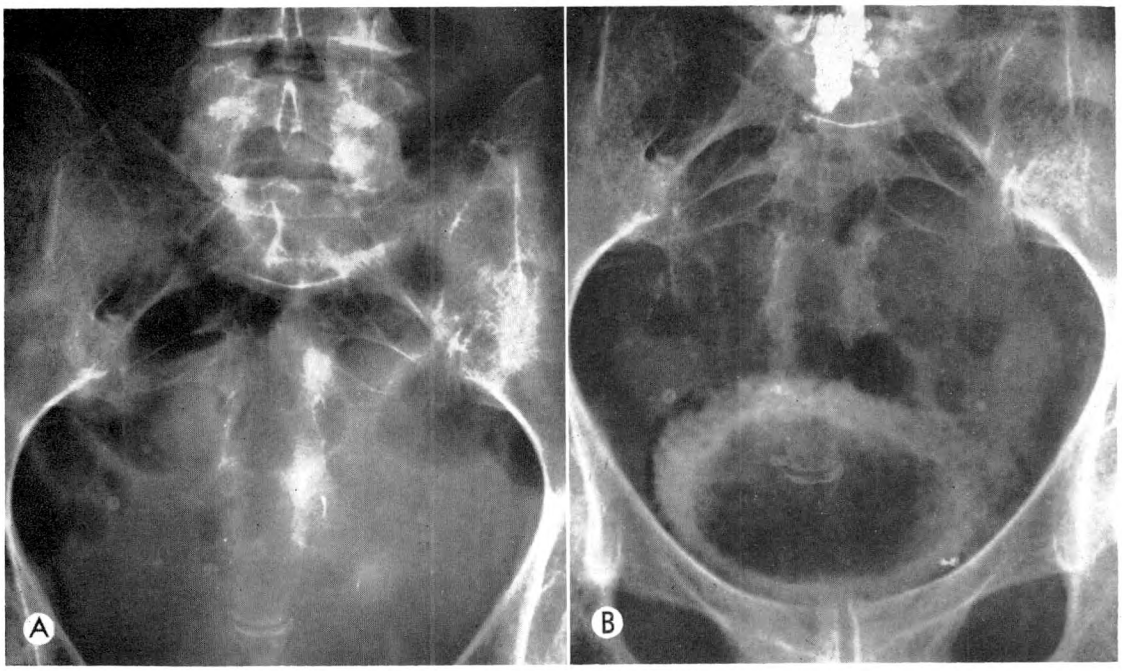


FIG. 1. Case 1. (*A*) Plain roentgenogram of the bladder region before discovery of cystitis emphysematosa. The bladder is moderately distended but shows no evidence of gas. (*B*) Two weeks later. Characteristic appearance with vesicles seen in profile and "*en face*." Note also the collection of gas within the lumen of the bladder.

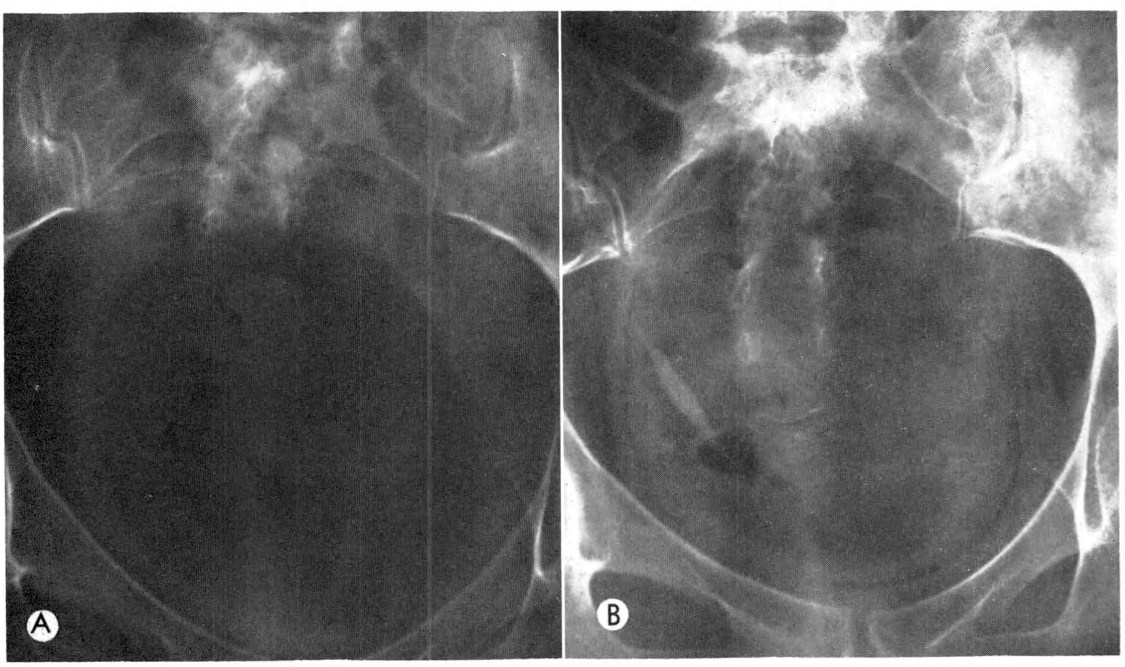


FIG. 2. Case 6. (*A*) Roentgenogram showing gas mainly within the lumen of the bladder. (*B*) Several minutes later after voiding most of the gas. The bladder wall can now be distinguished by the interstitial vesicles which were previously obscured by the larger collection of intraluminal gas.

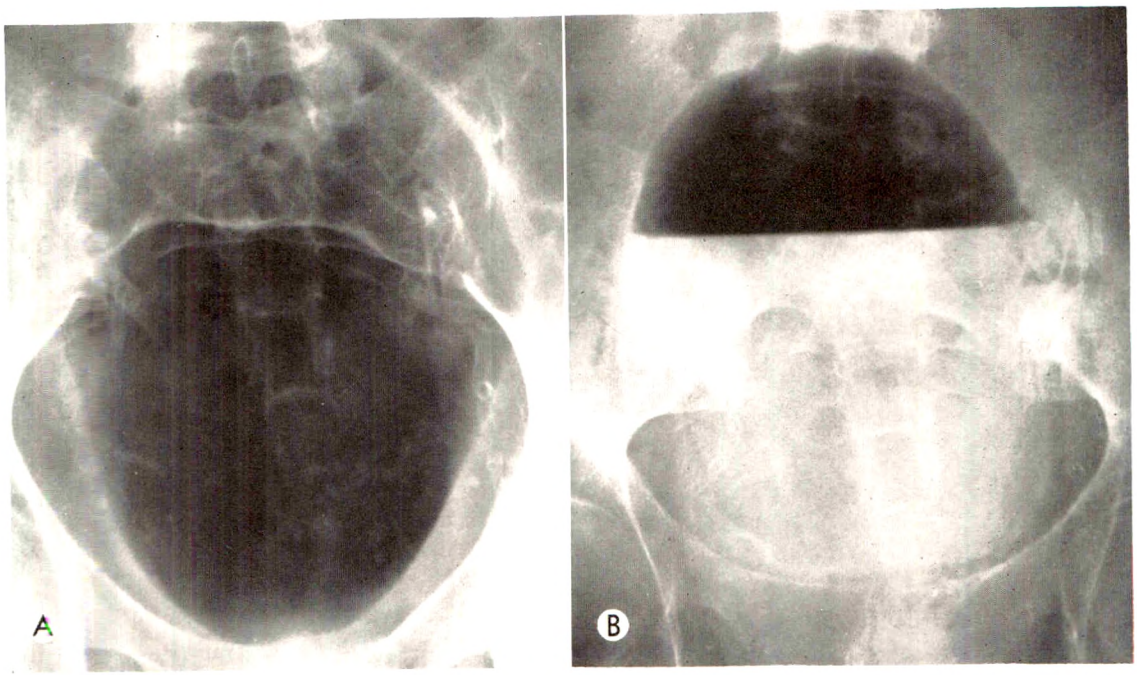


Fig. 3. Case 8. (*A*) Roentgenogram showing the distended gas-filled bladder extending almost to the level of the umbilicus. (*B*) Erect roentgenogram showing the characteristic air-fluid level.

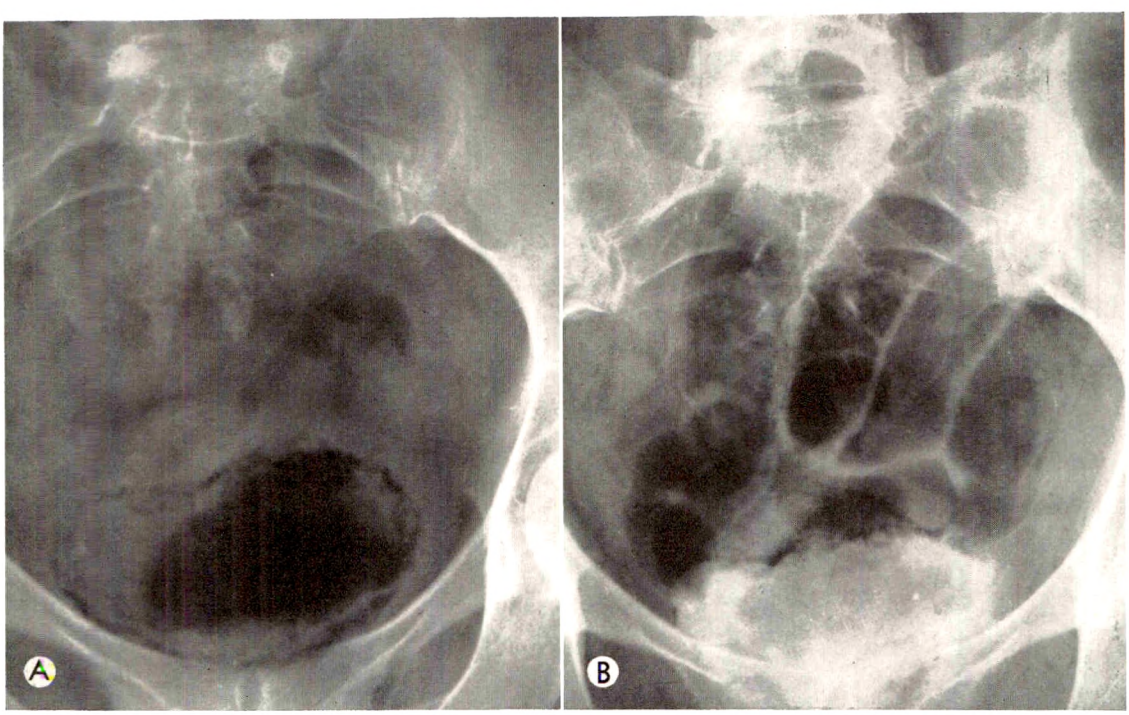


Fig. 4. Case 11. (*A*) Plain roentgenogram prior to intravenous pyelography. Characteristic interstitial vesicles and intraluminal gas bubbles are seen. (*B*) Intravenous post-voiding pyelogram showing slight depression of the bladder base and residual urine.

cases in the previous eight years. It should be noted that our hospital population of approximately 10,000 patients per year includes at least 3,000 diabetics. The proportion of diabetic admissions has remained relatively constant, although the incidence of patients with cystitis emphysematosa has apparently increased. It is noteworthy, in this respect, that in the series of necropsy cases reported by Mills,[20] in 1930, glycosuria was not a conspicuous feature. Nevertheless, in the recent literature most of the reported cases have had glycosuria, usually due to diabetes mellitus, as a notable feature of the disease, and, in general, the incidence of glycosuric cases in the early literature, although much higher than in the general population, was not so high as in cases reported during the last ten years. It is possible to explain this on several grounds. First, glycosuria is not an essential prerequisite for the development of gas in the bladder. However, infection is definitely necessary. Chronic, refractory urinary tract infections were much more prevalent in the pre-antibiotic era and all of the nondiabetic cases reported here have had evidence of long standing urinary infections. Since the advent of antibiotic therapy, moreover, patients with diabetes mellitus have formed a hard core of cases in which urinary tract infections are, because of the glycosuria, difficult to control, and when apparently controlled tend to recur readily. Similar infections in nondiabetic patients would be more amenable to complete eradication. Secondly, at the time of the early reported cases, the detection and adequate control of diabetes was less advanced than at present and the longevity of diabetic patients was not nearly so great as now. Patients therefore did not live to develop the late complications, such as diabetic neuropathy involving the bladder which has been such a conspicuous and recurring feature of the cases presented here. Furthermore, the roentgen examination has led to the detection of many cases of cystitis emphysematosa, both in glycosuric and nonglycosuric patients which would otherwise have been overlooked. The fact that this condition is relatively transient has been stressed by Faingold *et al.*,[6] and is confirmed in this series; in 15 of our cases the diagnosis was unsuspected clinically and in the 6 cases with follow-up roentgenograms at least 4 showed disappearance of the gas within four days.

One of the present cases lends support to the thesis that, in addition to glycosuria, it is necessary to have an organism which has increased propensity for gas formation. The organism isolated from Case 8 showed marked increase in gas production in glucose over a randomly selected strain of a similar organism.

That the condition is a relatively benign one is evidenced by the fact that none of the patients in the present series died as a direct result of the local condition. One patient died indirectly as a result of the treatment of this and other infections, and another patient died remotely as a result of an *E. coli* septicemia in which the chronic bladder condition could probably be incriminated etiologically. Cystitis emphysematosa will, on occasion, clear merely by treatment of the glycosuria and without the administration of antibiotics. In glycosuric cases the mechanism of gas formation is believed to be due to fermentation of glucose with formation of carbon dioxide, together with butyric and lactic acid. All of our diabetic cases except 2 showed an acid urine, whereas 3 of the 4 nondiabetic cases showed an alkaline urine. In the nondiabetic cases, the production of gas is thought to be due either to the breakdown of an abnormal albumin in the urine or else to the presence of a strain of *E. coli* which is capable of acting on normal albumin.

Clinically, the disease is of importance since the fermentation of glucose leads to a false low reading on urine testing, which therefore does not accurately reflect the blood sugar levels. This can lead to a vicious cycle of poor control, higher urine glucose levels, further infection leading onto further fermentation. Since the patient is infrequently aware of pneumaturia or

rarely reports it, the radiologist may be the first to break the cycle.

Finally, it is important to stress the fact that the presence of gas in the wall of the bladder and gas in the lumen of the bladder are manifestations of the same underlying etiologic factors. It has not been possible to determine from the cases studied here whether the gas in the lumen of the bladder is derived from rupture of vesicles or whether it is generated in the lumen itself. It may well be that both mechanisms are in operation at the same time. It would seem that, in order to avoid confusion, the condition should be referred to as "cystitis emphysematosa" and that the term pneumaturia, which is merely a description of a symptom, should be abandoned.

SUMMARY

The literature on "cystitis emphysematosa" and "pneumaturia" has been briefly reviewed. Findings in 19 additional cases are presented.

The high incidence of glycosuria and infection with gas-producing coliform organisms (*E. coli* and *Aerobacter aerogenes*) is stressed, together with the presence of urinary stasis.

The diagnosis is readily overlooked clinically and is essentially a roentgenologic one. The importance of the condition with regard to the control of diabetes is emphasized.

"Cystitis emphysematosa" and "pneumaturia" would appear to be manifestations of a single problem and it is proposed that the single term "cystitis emphysematosa" should be used to avoid confusion.

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The author wishes to thank Dr. Joseph H. Marks and Dr. Mirle A. Kellett for much valuable advice and criticism in the preparation of this paper.

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BULLOUS EDEMA OF THE BLADDER SIMULATING TUMOR*

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MANY pathologic conditions of the urinary bladder may be suggested by the appearance of the bladder in excretory urography. These include diverticula, extravasation, stones, trabeculation, abnormal capacity, and tumors. There are also many filling defects simulating tumor, such as those caused by foreign bodies, soft radiolucent stones, blood clots and "catheter edema." The latter, edema of the bladder dome caused by continued contact with a Foley catheter tip and bag, is a relatively common finding. However, a recent review of the American literature and of several well known urologic texts discloses no mention of this entity.[1–6]

Patients on constant Foley catheter drainage maintain an empty bladder, thus causing the catheter tip and bag to contact the posterolateral and superior surface of the bladder. This may lead to localized bullous edema which, when seen on the urogram, usually appears as a large sharply defined filling defect in the dome with irregularity of neighboring mucosa simulating carcinoma of the bladder.

Bullous edema is an inflammatory change of the bladder mucosa seen in acute cystitis. The mucosa appears irregularly thickened, inflammed, and rigid, and it is covered by multiple small, rounded, cyst-like elevations resulting from obstruction of the lymphatic channels and submucous effusion. Because of the difficulty in differentiation from tumor we are presenting several examples of this entity. It is important to be aware of the possibility of "catheter edema," although tumor must still be considered in the differential diagnosis.

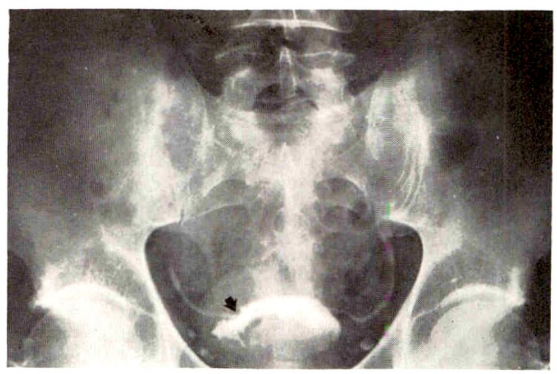


FIG. 1. Case I. Excretory urogram showing defect (arrow).

REPORT OF CASES

CASE I (Fig. 1). A seventy year old white man was admitted to the Urology Service with signs and symptoms of prostatism. The patient was in acute urinary retention and was catheterized on the day of admission. The Foley catheter was in place for four days prior to excretory urography. The roentgen report stated, "In the region of the right ureteropelvic junction, on the superior margin of the bladder, there is a definite semilunar shaped filling defect associated with irregularity of the bladder wall. The findings here are consistent with a neoplasm of the bladder and should be further studied."

At the time of transurethral resection of the prostate, cystoscopy revealed bullous edema in this area with no evidence of tumor.

CASE II (Fig. 2). A sixty-eight year old male Negro was admitted to the Urology Service with the diagnosis of benign prostatic hypertrophy. The patient had had an indwelling Foley catheter for three weeks prior to excretory urography. The roentgen report stated that the "bladder has an irregular outline, especially on the left side, suggesting the

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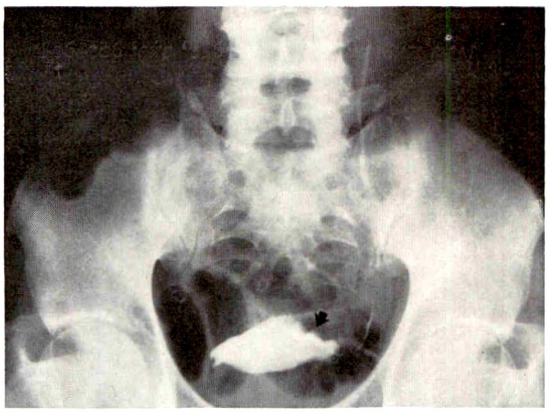


Fig. 2. Case II. Excretory urogram showing defect (arrow).

possibility of an intrinsic neoplasm of the bladder."

Cystoscopic examination revealed bullous edema, most marked on the posterior superior surface of the bladder on the left.

Case III (Fig. 3). A seventy year old white male was admitted to the Urology Service in acute urinary retention. He was placed on Foley catheter drainage for five days prior to excretory urography. Again the defect was noted and the possibility of bladder tumor was suggested.

Cystoscopy revealed the area to contain bullous edema, and there was no evidence of bladder tumor.

Case IV (Fig. 4). A sixty-nine year old male Negro was admitted to the Urology Service in urinary retention with a Foley catheter which had been in place for three weeks. Excretory urography revealed poor filling on the left side of the bladder suggestive of tumor.

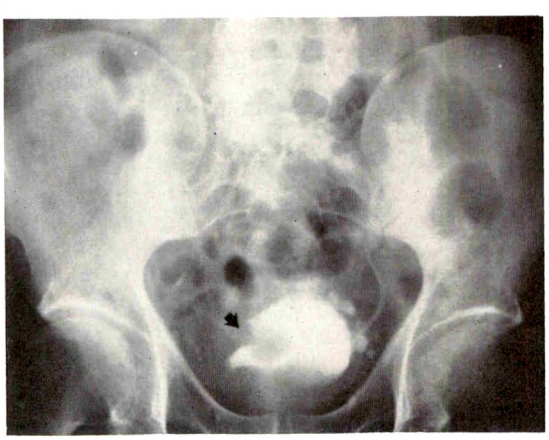


Fig. 3. Case III. Excretory urogram showing defect (arrow).

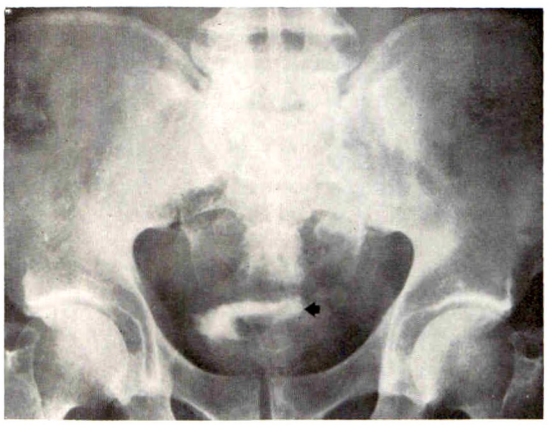


Fig. 4. Case IV. Excretory urogram showing defect (arrow).

This area was found to be edematous at the time of cystoscopy and no evidence of bladder tumor was seen.

Case V (Fig. 5). A seventy year old white male was admitted to the Urology Service with signs and symptoms of outlet obstruction. Because of a large amount of residual urine, a Foley catheter was put in place and was present for four days prior to excretory urography. The roentgen report of the pyelogram revealed "marked irregularity of left uretero-vesical junction which could represent a bladder tumor."

Cystoscopy demonstrated edema surrounding both ureteral orifices, most marked on the left. No evidence of bladder tumor was found.

COMMENT

All excretory urograms were made prior

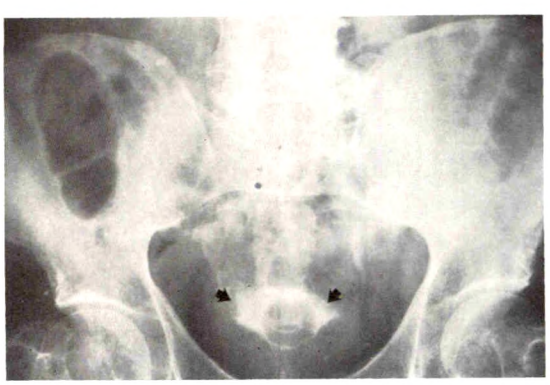


Fig. 5. Case V. Excretory urogram showing defects at both ureteral orifices (arrows).

to transurethral resection. The 5 cases described above showed the characteristic changes of bullous edema. All of the cases presented a similar roentgen appearance, *i.e.*, a sharply defined filling defect in the superolateral portion of the bladder dome, the area where the catheter bag most frequently rests. The findings were constant and readily seen on all urograms in which the bladder was filled with contrast material.

Each of the patients reported was admitted to the urologic service with a diagnosis of benign prostatic hypertrophy. All had been on Foley catheter drainage for lengths of time varying from four days to one month. They were cystoscoped prior to transurethral resection of the prostate gland and in all cases the described filling defects and prominent folds were caused by bullous edema. The mucosa was seen to be pale and swollen and it "pitted" readily when the loop of the resectoscope was pressed into the area. In no instance was there a suggestion of tumor and biopsy was not deemed necessary by the surgeon. None of the patients had clinical evidence by history or urinalysis of either gross or microscopic hematuria prior to catheterization.

SUMMARY

Several cases of bullous edema of the bladder caused by continuous contact with a Foley catheter are reported. The importance of this finding is noted in view of the relative frequency of its occurrence and of its resemblance to bladder tumor.

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GYNECOGRAPHY

TECHNIQUE AND INTERPRETATION

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ROENTGENOGRAPHIC visualization of the structures in the female pelvis by intraperitoneal gas contrast study was first described by Goetze,[7,8] in 1918. Utilization of this technique is occasionally reported in the literature.[1,2,5,6,9,14,15,16,17] However, few radiologists and other clinicians resort to this technique in the diagnostic evaluation of the pelvis or abdomen, mainly because of fear of gas embolism. This fear appears quite unwarranted with choice of proper gas and technique. Indication for this procedure, preparation of the patient, equipment, technique, problems and complications, as well as interpretation will be discussed.

Initially, gynecography was done at the Clinical Center of the National Institutes of Health as part of the evaluation of patients with Stein-Leventhal syndrome[18]. Subsequently, other abdominal and pelvic diagnostic problems in patients ranging from two to seventy-two years of age have been evaluated by this procedure. This very informative test is simple and safe; it may be performed on outpatients, even women weighing 300 pounds.

PREPARATION AND POSITIONING OF THE PATIENT

Careful preparation is the cornerstone of a successful study. A cathartic, preferably castor oil, is given on the day preceding the examination. In the morning the patient has nothing by mouth. A cleansing enema is given one to two hours before reporting to the radiology department. The patient is instructed to empty her bladder "completely" just before the procedure itself is begun. If adequate preparation is questioned, a scout roentgenogram of the lower abdomen may demonstrate a distended bladder or a scybalous rectosigmoid colon.

The patient is placed supine on a standard roentgenographic tilt table that has a footboard and shoulder rest. Her feet are secured to the board by a boot and strap arrangement of the type used in myelographic procedures. Improvisation with broad adhesive tape as used in leg traction will, however, suffice (Fig. 1, *A*, *B*, and *C*).

MATERIALS

To properly perform gynecography, the following materials are necessary:

- Stand
- Gloves
- Sterile peritoneal puncture tray
  - Sponges and spongestick for skin preparation
  - Towels (4)
  - Syringes, ml. (2)
  - Needles, 22 gauge, 1 inch (2)
    20 gauge, 2 inch spinal (1)
    20 gauge, 3½ inch spinal (2)
    20 gauge, 6 inch spinal (1)
  - Tubing, latex, two sections, each approximately 2 feet long
  - Glass tube connector, Y-shaped
  - One way stop cock, syringe adapter
  - Small hemostat (1)
  - Medicine cups (2)
- Xylocaine, 1 per cent
- Sterile saline or water
- Antiseptic solution or tincture
- Tank of nitrous oxide with attached flowmeter, as used in anesthesia apparatus (separate nitrous oxide flowmeters are available from anesthesia equipment manufacturers)

The two sections of tubing are connected by the Y-tube glass connector; one open end of the rubber tubing is attached to the flowmeter of the nitrous oxide tank. The stop cock is connected to the other open end

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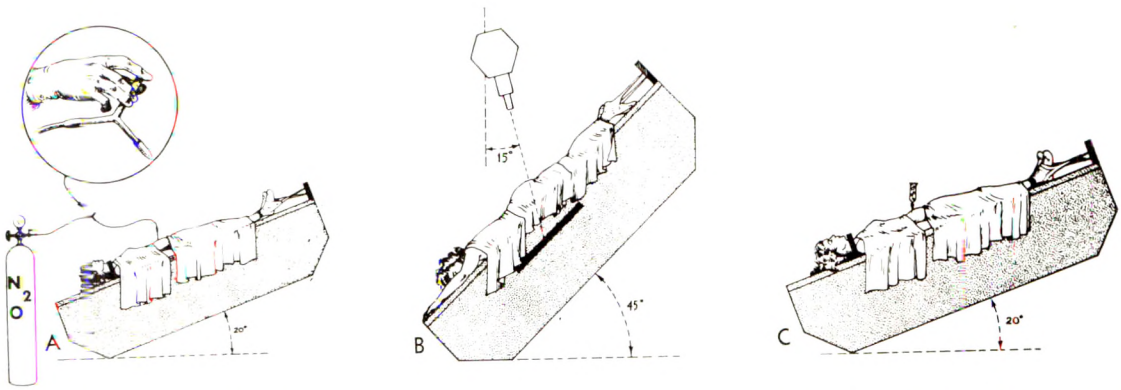


Fig. 1. In sequence these drawings demonstrate (*A*) positioning of the patient during establishment of pneumoperitoneum (note glass connector valve arrangement), (*B*) positioning of patient and equipment during roentgenography, and (*C*) positioning during removal of the gas from the peritoneal cavity (note gas bubbling through the fluid in the syringe).

of the tubing. This entire system is carefully checked for leaks by occlusion of the free end of the Y-tube glass connector.

Establishment of Pneumoperitoneum

Following preparation of the skin with antiseptic solution, the abdomen is draped with towels, leaving a small portion of the para-umbilical area exposed. Local anesthesia, 2–4 cm. to the left and below the umbilicus, precedes the peritoneal puncture which is made with a spinal needle of proper length. In patients having left sided scars or masses, a corresponding puncture site is chosen on the right; right sided punctures have been found equally sucessful. A 2 inch needle is used on the average patient. Obese women generally require a needle $3\frac{1}{2}$ inches long; the 6 inch needle has been used only twice, each time on a patient weighing over 300 pounds. The needle is slowly advanced until it enters the peritoneal cavity. In most instances it is not difficult to realize when this has occurred. Two distinct "pops" are felt as the needle is advanced: the first may be related to puncture of the fascial plane anterior to the preperitoneal fat, and the second signals entrance into the peritoneal cavity itself. The obturator is removed for inadvertent blood vessel penetration check by syringe (which we have never observed). If no blood is aspirated, the needle is secured by a hemostat resting on the abdominal wall. The table is then tilted 20–25 degrees, headdown.

The stopcock is connected to the spinal needle and opened to the gas line. Flow rate of nitrous oxide is set at 600 ml./min. Timing of gas flow is begun when the radiologist closes the system from tank to patient by occluding the open limb of the Y-tube glass connector with his gloved finger. After a few seconds and several times thereafter during the filling period, pressure is checked by momentary lifting of the finger from the open Y-limb. Only a gentle hissing sound should be heard. A louder noise by the escaping gas indicates increased pressure in the system and mandates repositioning of the needle before proceeding. Two to three thousand milliliters of nitrous oxide are introduced into the peritoneal cavity over three to five minutes. The exact volume used is determined by the patient's size and by the tone of her abdominal wall.

The patient is tilted head-down during filling to prevent abdominal discomfort and shoulder pain resulting from subdiaphragmatic gas accumulation. With this precaution the patient should experience nothing more than increasing abdominal "fullness." If complaints of pain do occur, one can be fairly certain that the needle is improperly positioned and that repeat

peritoneal puncture is indicated before proceeding.

ROENTGENOGRAPHIC TECHNIQUE AND FOLLOW-UP

When the patient has no pain during filling, the total intended volume of gas is delivered, the stopcock closed, the needle removed, and the patient turned into the prone position. Table tilt is increased to 45 degrees head-down. The roentgen-ray tube is angled 15 degrees from the vertical towards the feet, resulting in a 30 degree pelvic inlet projection. Gynecograms are obtained in the posteroanterior and both oblique projections with the central ray entering 3 to 5 cm. below the tip of the sacrum. When the posteroanterior gynecogram furnishes the desired information, the other exposures can be omitted. Occasionally, special problems require other angles and projections.

The technical factors used are: 40 inches target film distance, conventional film and par screens, Bucky grid (8:1 ratio), either phototiming at S-1 selector or 30 to 60 mas., 60–80 kv.

After satisfactory (wet reading) gynecograms have been obtained, the patient is turned back into the supine position and the table tilt is reduced to 20 to 25 degrees. Peritoneal puncture is again performed through the same anesthetized site, a syringe containing 1 ml. of sterile saline or water is attached and the plunger is removed. When bubbling of the escaping nitrous oxide has ceased, the needle is removed and the patient helped from the table. We have our patients lie recumbent for two to three hours before returning home; but this precaution is not essential. Occasionally, a patient will complain of shoulder ache on sitting; this disappears by morning and has not required the use of analgesics. In general, no follow-up observation is necessary.

The above described technique has been found safe and well tolerated in patients ranging from two to seventy-two years of age.

COMPLICATIONS AND PROBLEMS

Cautious, slow and gentle manipulation of the needle is a good way to prevent complications. No serious complications were encountered. Respiratory embarrassment was never a complaint. In one instance gas was introduced into the small bowel (Fig. 7), but the patient experienced no discomfort of any kind and remained asymptomatic over the succeeding days. Physical examination showed promptly subsiding distention. This patient was known to have had suppurative peritonitis with surgical drainage two years earlier, and widespread adhesions were the likely cause of small bowel puncture.

All our problems, minimal and few as they are, derive from improper needle placement. In the very obese or very muscular patient, the previously described sensation of "popping," when resistance is overcome, is not clearly discernible, and preperitoneal needle positioning may result. In the very thin patient inadvertent puncture of the retroperitoneal space is possible. These extraperitoneal insufflations cannot be detected reliably by manometric measurement or by noting of flow rate and resistance with the injection of a few milliliters of sterile fluid. Auscultation of the abdomen during insufflation is sometimes helpful, particularly in the small or normal sized patient; a distinctive hissing may be heard when gas freely enters the peritoneal cavity. The most reliable criterion for improper needle placement and extraperitoneal insufflation is the patient's complaint of discomfort. This takes the form of radiating pain toward the flanks or epigastrium, usually within a few seconds of the onset of gas flow. For the occasional stoic patient even this criterion fails. In such a case, and, in general, if there is some question of the exact needle position, an anteroposterior scout roentgenogram of the abdomen is taken. With perfect intraperitoneal injection, gas sharply delineates the peritoneal cavity inferiorly and laterally (Fig. 2). Preperitoneal extravasation of gas is diagnosed by the mottling that is charac-

teristic of interstitial emphysema; in the pelvis this mottling is noted surrounding the bladder (Fig. 3, 4 and 5). With retroperitoneal infiltration, linear dissection of gas is found along the psoas shadows (Fig. 6).

Extravasation of gas outside the peritoneal cavity occurs infrequently and has caused no complications. Slight discomfort is induced but absorption of small amounts of nitrous oxide from interstitial tissues is complete within about two hours. When gas is not removed from the peritoneal cavity proper after the gynecograms have been taken, complete absorption requires up to forty-eight hours. In this event, shoulder ache upon assumption of the upright position is a common complaint. The advantageous use of nitrous oxide merits brief mention. Teschendorf[20] has shown, and it is well known, that carbon dioxide and nitrous oxide are "safe" gases that are quickly diffused and absorbed. Resorption time of these two gases is approximately twenty times faster than that of oxygen.

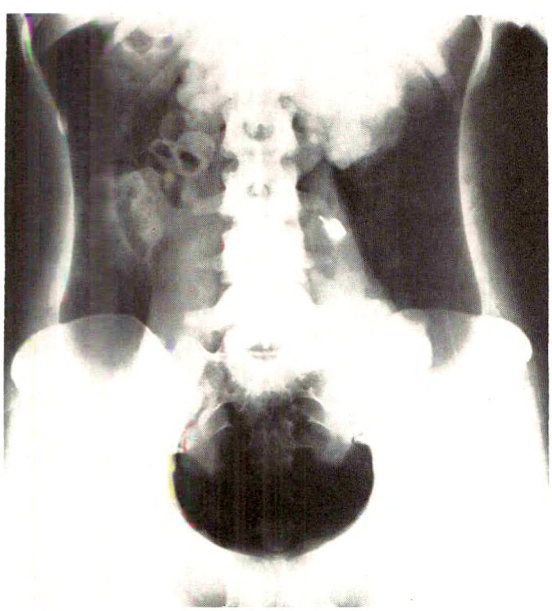


Fig. 2. (29144). Anteroposterior scout roentgenogram demonstrates sharp delineation of the peritoneal cavity laterally and inferiorly after proper gas insufflation. (Figure 1*A* shows the position of the patient and the table; the central ray enters perpendicularly to the table).



Fig. 3. (30338). Gynecogram shows interstitial emphysema due to preperitoneal extravasation of gas (arrows). Note the clear delineation of the urinary bladder by the surrounding gas. Repositioning of the needle resulted in good intraperitoneal gas contrast with effective visualization of the pelvic organs.

The ratio is even greater when compared to air. Carbon dioxide and nitrous oxide are nontoxic. Although carbon dioxide is absorbed slightly faster than nitrous oxide, the latter gas is less irritating and for this reason is preferred in our department.

Interpretation of Gynecograms

Well performed gynecography reveals the pelvic organs with unusual clarity. Roentgen findings in an anatomically normal pelvis (Case 1) are shown in Figures 8 and 9.

Case 1 (28882). A thirty-two year old subject with Cushing's syndrome had normal menses, no abnormal findings on pelvic examination and a normal endometrial biopsy. At laparotomy for bilateral adrenalectomy, the ovaries and uterus were unremarkable. The pathologic diagnosis was adrenocortical hyperplasia. Ovarian biopsies were normal.

Anteriorly, the smooth shadow of the col-

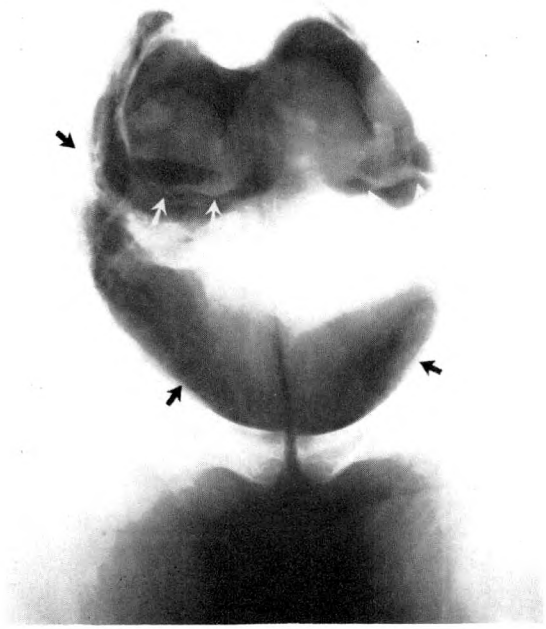


FIG. 4. (28713). Gynecogram shows partial preperitoneal extravasation (black arrows) in a patient with normal ovaries and uterus. Note excellent visualization of the round ligaments (white arrows).

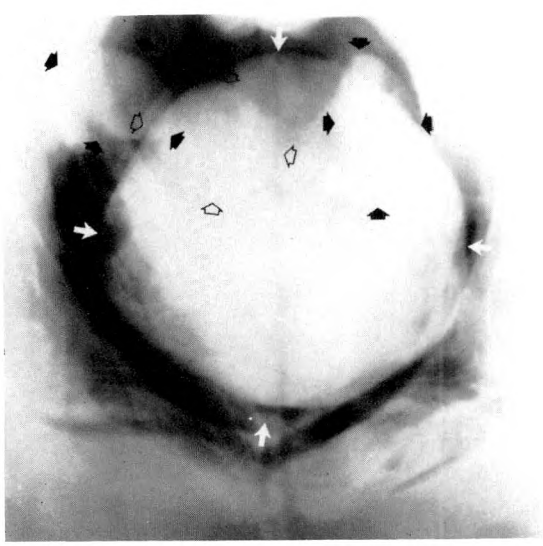


FIG. 5. (24591). Gynecogram shows extensive preperitoneal gas extravasation. Note the faint visualization of the enlarged ovaries (black arrows) and of the uterine fundus (outlined arrows) and the clear delineation of the bladder (white arrows).

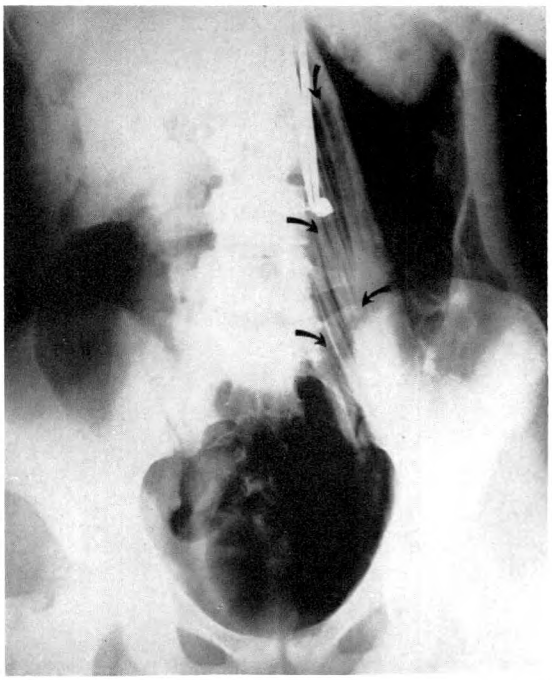


FIG. 6. (29595). Gynecogram shows retroperitoneal gas extravasation causing linear dissection of gas along the psoas muscles (arrows).

lapsed bladder was readily recognized on the gynecogram. Both adnexal regions were smooth and free of masses. The uterine fundus was seen in the midpelvis, with its density superimposed on that of the cervix. Bilaterally, the curvilinear shadows of the round ligaments branched away from the broad ligaments anteriorly. The fallopian tubes with their thickened fimbriated ends were seen intimately associated with the ovarian shadows in the superior lateral aspect of the broad ligaments. The ovaries themselves were posterolateral to the uterine fundus; their precise location relative to the fundus was variable and changed with shifting position of the patient. The collapsed rectosigmoid reflection extended posteriorly and along the pelvic rim to the left and upward into the abdomen.

The size of the pelvic organs is readily determined from the measurements made on the posteroanterior and both oblique gynecograms. The width of the uterine fundus is conveniently measured from isthmus to isthmus. The fundus thickness is determined perpendicular to this interisthmus line on the posteroanterior film. The ovarian length is the longest dimension on the



Fig. 7. (27055). Gynecogram shows accidentally introduced gas in the small bowel of a diabetic patient who had had suppurative peritonitis and surgical drainage two years earlier. This caused no symptoms or sequelae.

posteroanterior or either oblique gynecogram. The measurement of the greater dimension at right angle to this long axis yields the ovarian width; the lesser perpendicular dimension is the ovarian thickness. All measurements should be corrected for distortion by decreasing the numbers by 20 per cent on patients of average girth and by 25 per cent on obese patients.

In cases where gynecographic measurements were checked at laparotomy, correlation was good and the greatest discrepancy only once exceeded 1.0 cm. In most instances, roentgenographic measurements varied by no more than a few millimeters from the dimensions recorded at operation.

The pelvic viscera of normal females of child bearing age vary considerably in size. Standard textbooks of anatomy[13] and obstetrics[4] record normal ovaries measuring 2.5 to 5 cm. in length, 1.5 to 3 cm. in width and 0.7 to 1.6 cm. in thickness. An even greater range is given for dimensions of the normal nongravid uterus. Despite this variation in size of the viscera themselves, the *ratio* of the uterine fundus width to the ovarian length is consistently greater than 1.0 cm. and usually greater than 1.3 cm. in the normal pelvis.

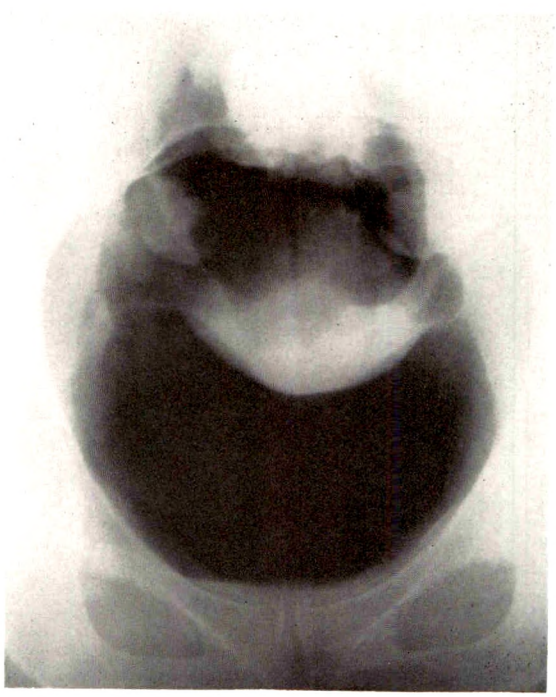


Fig. 8. Case 1 (28882). Normal posteroanterior gynecogram (see Fig. 1*E*).

In this hospital, gynecography has been used frequently in the evaluation of patients with the polycystic ovary syndrome. This entity, first described by Stein and Leventhal[18] in 1935, was recently reviewed by Stein.[19] Pertinent features are the his-

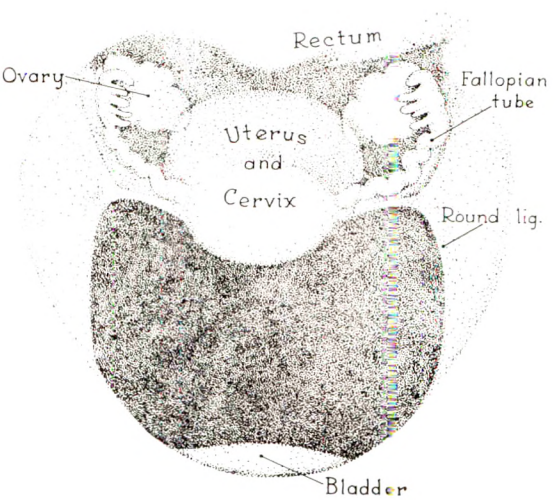


Fig. 9. Case 1 (28882). An illustrative drawing of Figure 8 is presented since copying and recopying of the original gynecogram tends to obscure detail.

tory of menstrual irregularities (especially oligomenorrhea or amenorrhea) and the finding of bilaterally enlarged ovaries, uterine hypoplasia in 75 per cent and hirsutism in about 50 per cent of the cases. Virilization is absent. Stein and Leventhal recognized at the outset that the ovarian enlargement, crucial to the diagnosis, could not be established in about half of their patients by physical examination alone. Using gynecography, however, they were able to demonstrate unequivocal ovarian enlargement in all cases. Gynecograms also delineated the typically small uterine fundus. These authors called attention as well to the usefulness of the ratio of the ovarian to the uterine size. In their experience the normal ovary was one-fourth to one-half the size of the uterine fundus, whereas the polycystic ovary was at least three-fourths as large as the uterine shadow.

Gynecograms of a typical case of the Stein-Leventhal syndrome[18] (Case II) are shown in Figure 10, *A*, *B* and *C*. Figure 10*D* shows another patient with the same syndrome.

CASE II (22002). An eighteen year old girl, complaining of hirsutism, oligomenorrhea and obesity, had a small uterus but no suggestion of ovarian enlargement on physical examination. At laparotomy the ovaries were found to be large and cystic. The microscopic findings were compatible with those described by Stein and Leventhal (cf. Stein review). Gynecographic demonstration of the ovarian enlargement relative to the small uterine fundus was the decisive factor leading to exploration.

Ovarian enlargement in the polycystic ovary syndrome is described as bilaterally symmetric (Stein review). We have confirmed this finding in all but one of our patients with this entity. This patient (Case III) had bilateral ovarian enlargement but the enlargement was asymmetric (Fig. 11). Gross and microscopic findings were typical of those described by Stein and Leventhal.

CASE III (27726). A twenty year old student nurse had menarche at the age of eleven, oligomenorrhea from the age of eleven to sixteen and menorrhagia for the next two years, followed by progressive oligomenorrhea. At the time of her admission she had been amenorrheic for seven months. Severe acne and moderate hirsutism were apparent on physical examination but her habitus was female, her breasts well developed and her clitoris normal in size. The right ovary was enlarged, questionably cystic and very tender to palpation. The left ovary was felt to be somewhat smaller but was also tender. The twenty-four hour excretion of 17 ketosteroids was normal. Surgical exploration revealed a right ovary measuring 5.0×3.5×2.8 cm. and a left ovary measuring 3.7×2.9×2.4 cm. Bilateral wedge resections were performed. Microscopically, the ovarian wedges showed an extremely thick and fibrous tunica, subcapsular cysts, no corpora lutea and only one corpus albicans.

Ovarian enlargement of the Stein-Leventhal syndrome is not associated with adnexal abnormalities, attachment of the ovaries to the adnexa, or abnormal configuration of the broad ligaments (Fig. 10, *A–D*; and 11). One patient (Case IV) with suspected polycystic ovaries was found at gynecography to have symmetric bilateral ovarian enlargement, but the ovaries were attached to irregular and thickened adnexal regions (Fig. 12).

CASE IV (18266). A twenty-eight year old Negro woman had oligomenorrhea, infertility and a history of a vaginal discharge ten years earlier for which she had been treated with penicillin. The uterus and adnexal areas were normal to palpation. She was not hirsute. Serology was negative. Urinalysis and renal function were normal. The preoperative diagnosis was probable Stein-Leventhal syndrome. At surgery she was found to have chronic pelvic inflammatory disease in addition to polycystic ovaries. Hysterosalpingograms made after surgery demonstrated patency of the right and obstruction of the left fallopian tube; numerous diverticula arose from each fallopian tube.

The usefulness of gynecography is well demonstrated in another patient (Case V) suspected of having the polycystic ovary syndrome (Fig. 13, *A*, *B* and *C*).

CASE V (29922). This twenty-seven year old white woman had oligomenorrhea, infertility,

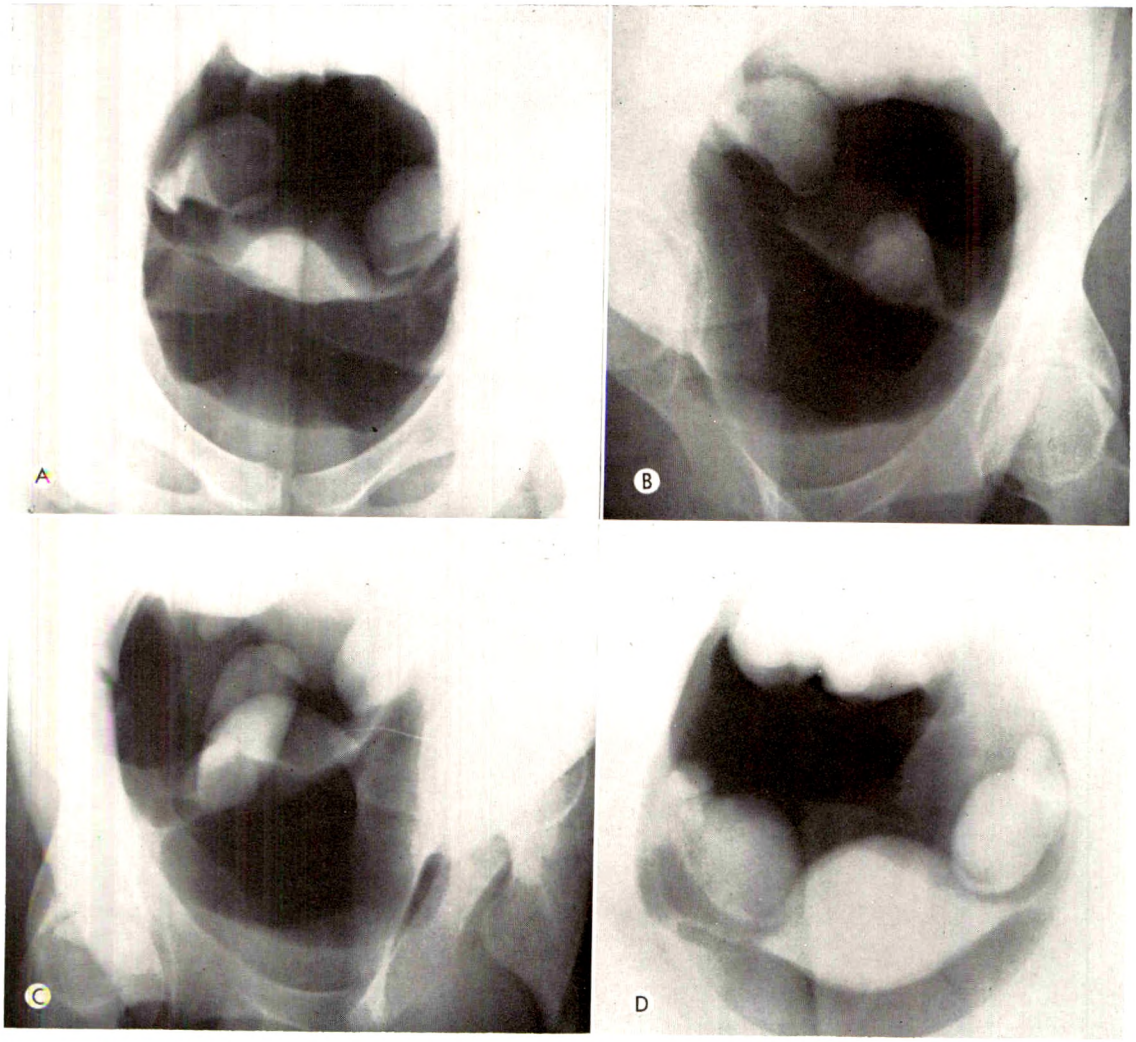


Fig. 10. Case 11 (22002). Stein-Leventhal syndrome. Posteroanterior (*A*), right anterior oblique (*B*) and left anterior oblique (*C*) gynecograms demonstrate large, thick ovaries and a relatively small uterine fundus. Note the smooth bladder shadow anteriorly, the collapsed rectosigmoid colon posteriorly, the cervical shadow superimposed upon the fundus shadow and the sharp delineation of the fallopian tubes. In the oblique studies (*B* and *C*), note the shift of the ovaries with the shift of the patient. (*D*) (31161). Gynecogram shows excellent visualization of the enlarged ovaries and of the uterus in another patient with the Stein-Leventhal syndrome. Note the fimbriated ends of the fallopian tubes.

and hirsutism. There was no history of venereal disease or abdominal surgery. Pelvic examination was unsatisfactory; the ovaries were not readily palpable but considered to be somewhat large. One senior observer felt "right adnexal fullness." She was sent to the radiology department with the diagnosis of Stein-Leventhal syndrome.

Gynecograms (Fig. 13, *A*, *B* and *C*) demonstrated a large pelvic mass, adherent to the right adnexa, widened and tortuous uterine ligaments bilaterally (fallopian tubes), a fixed, lobulated, slightly enlarged left ovary and a uterus that was small but probably within normal limits in size. A hysterosalpingogram (Fig. 14) showed the changes of bilateral old tubal inflammatory disease. At laparotomy bilateral chronic pelvic inflammatory disease was evident. Peritoneal adhesions, thickened, fixed and tortuous fallopian tubes, a right ovarian tumor and a cystic, perhaps slightly enlarged, left ovary were noted during dissection. The right ovarian mass measured 6.5×4 ×3 cm.; histologic sections showed papillary

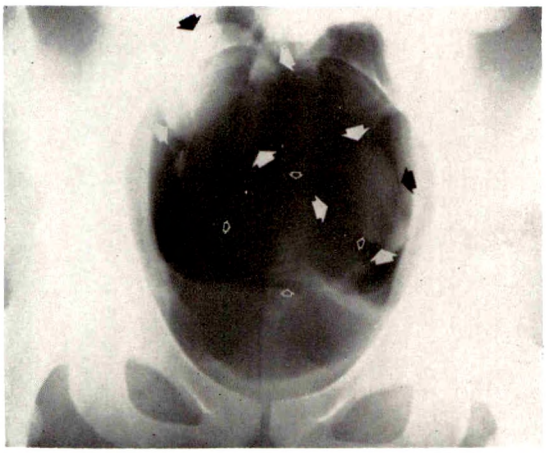


FIG. 11. Case III (27726). Gynecogram shows the ovaries of this patient with the Stein-Leventhal syndrome to be asymmetrically enlarged (large arrows). The small arrows delineate the uterine fundus.

cystadenoma. Multiple cysts were noted on incising the left ovary; the microscopic findings were considered compatible with polycystic disease. The roentgenologic findings contributed considerably to the management of this case. There was no clinical evidence for the pelvic inflammatory disease shown by gynecography and hysterosalpingography.

Generally speaking, interpretation of gynecograms done on patients who have had prior pelvic surgery is difficult. Postoperative adhesions often prevent the free entrance of gas into the pelvis and all but one of the gynecograms performed on such patients were technically below par.

Some difficulty is encountered as well in the reading of gynecograms where there is borderline enlargement of the ovaries in the presence of a relatively small uterus (Fig. 15); in such cases we recommend culdoscopy.

A gynecogram (Fig. 16) made of a fifteen year old girl (31339) who was suspected of having ovarian agenesis showed a very small cervix and very small and rudimentary genitalia, consisting of mere soft tissue ridges, extending toward both adnexal regions, and ending in oval shaped thickenings. This finding was not established by the rather unsatisfactory physical examination.

Figure 17 demonstrates ovarian enlargement, more marked on the left, and uterine enlargement in a thirty-two month old patient (31872). This precocious girl began to menstruate at the age of eleven months. Repeated rectal examinations were not revealing. Ovarian biopsies showed multiple follicular cysts.

Carcinoma of the cervix demonstrated by gynecography has been described previously.[1] Cervical, broad ligamental and adnexal changes due to tumor invasion were observed in patients studied primarily for measurements of "normal" ovaries.

Occasionally, other primary and metastatic tumors, particularly of the lower abdomen and pelvis, were successfully evaluated by gas contrast studies. Consideration of these cases is, however, beyond the scope of this paper.



FIG. 12. Case IV (18266). Gynecogram shows chronic pelvic inflammatory disease in this patient with the Stein-Leventhal syndrome. Note fixation of enlarged ovaries by adnexal adhesions (large arrows) and the small uterus and cervix (small arrows).

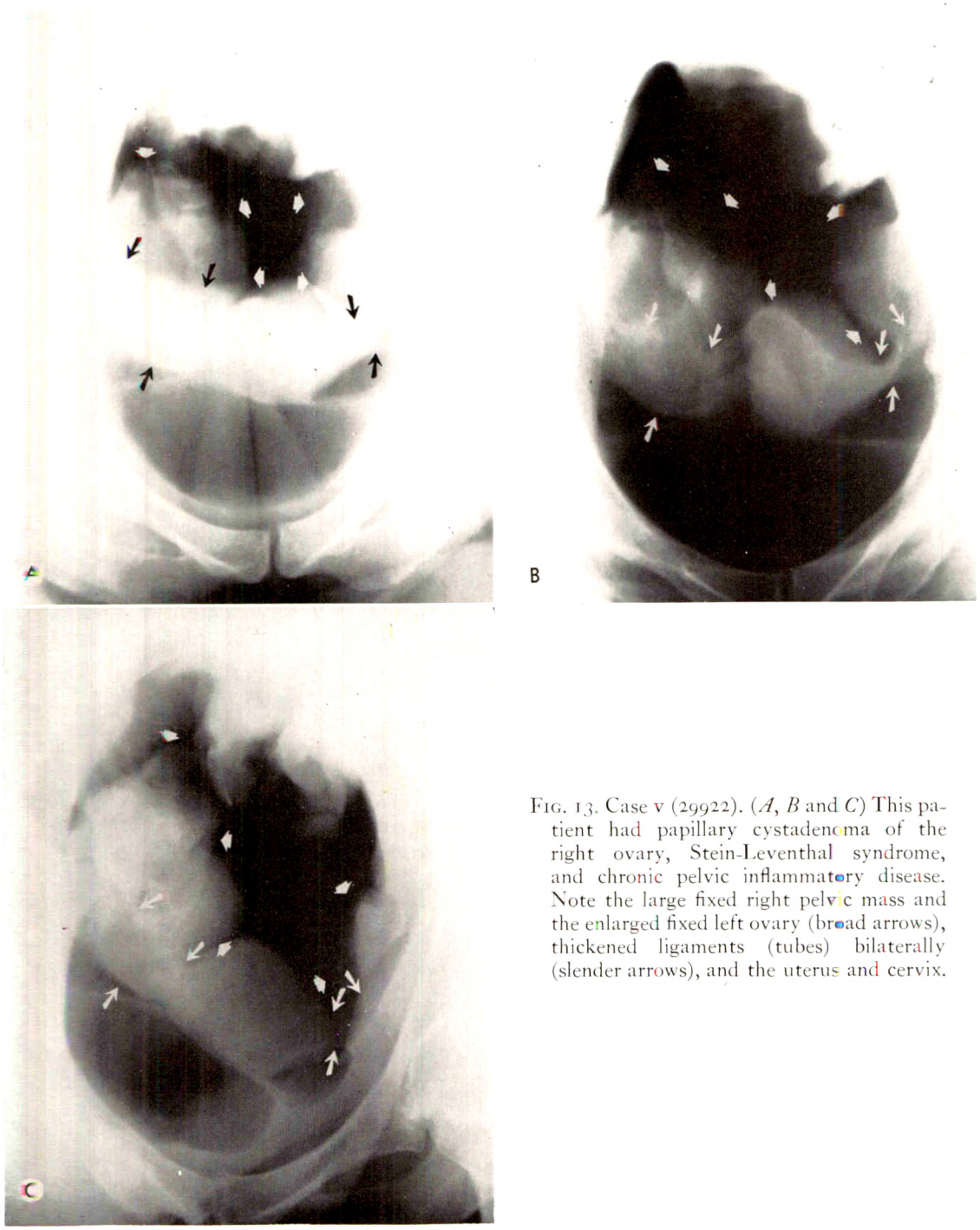


FIG. 13. Case v (29922). (*A*, *B* and *C*) This patient had papillary cystadenoma of the right ovary, Stein-Leventhal syndrome, and chronic pelvic inflammatory disease. Note the large fixed right pelvic mass and the enlarged fixed left ovary (broad arrows), thickened ligaments (tubes) bilaterally (slender arrows), and the uterus and cervix.

DISCUSSION

Gynecography is a simple but very useful technique in diagnosis. Using nitrous oxide as a contrast agent, the procedure carries a negligible risk of mortality and no cases of fatal gas emboli have been reported with this highly water soluble gas. Morbidity has been rare, transitory, and without sequel.

Excellent visualization of the pelvic

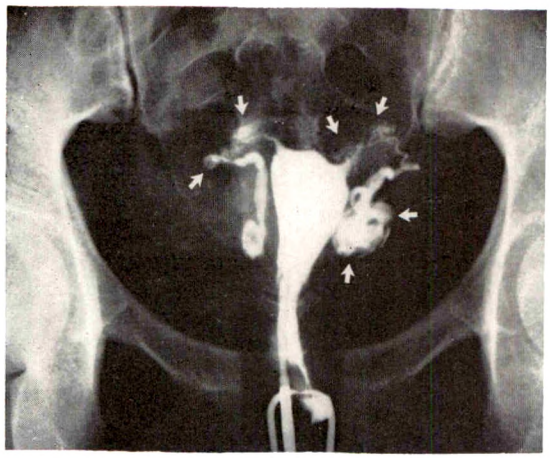


FIG. 14. Case v (29922). Hysterosalpingogram shows evidence of chronic inflammatory disease (arrows). Peritoneal spillage of contrast material on the right side was observed on a subsequent roentgenogram.

structures was achieved in all patients who had not undergone previous abdominal or pelvic surgery. In all but one of those who had had antecedent surgery, the gynecograms were still adequate for evaluation of ovarian and uterine size and configuration. The accuracy of pelvic organ measurement by this method was repeatedly confirmed at laparotomy.



FIG. 15. (28854). Gynecogram shows borderline enlargement (particularly thickening) of the ovaries. In such instances culdoscopy is suggested. Note a loop of sigmoid colon overlying the left ovary.

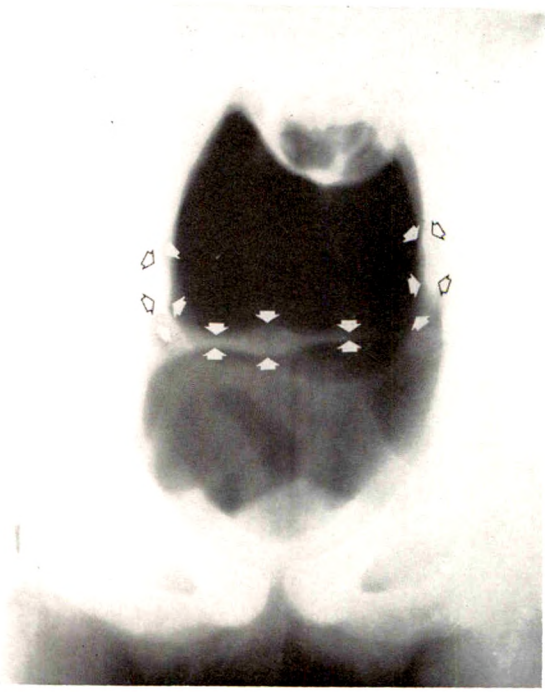


FIG. 16. (31339). Gynecogram shows ovarian agenesis in a fifteen year old girl. Note the rudimentary genital structures (arrows).

Gynecography is particularly useful in evaluating the pelvis of extremely obese or very young patients. In the former, physical examination, even under anesthesia, is often unrewarding. In children, the risk of general anesthesia is probably greater than risk of pneumoperitoneum—and the physical examination less informative than the roentgenogram. Gynecograms provide objective confirmation of positive physical findings and, notably in the polycystic ovary syndrome, will unearth ovarian enlargement missed by the clinician. We have been impressed as well with the opportunity to diagnose chronic pelvic inflammatory disease by roentgenography where there had been little or no clinical evidence to suggest such an entity.

Gynecography has been superseded in at least one large clinic[11] by culdoscopy, an

endoscopic procedure affording direct visualization of the pelvic contents. Even in experienced hands, however, the use of the culdoscope carries a certain morbidity.[12] It is our impression that this morbidity, however small, is greater than that associated with nitrous oxide pneumoperitoneum and hence we advocate gynecography as the initial screening procedure. This is particularly true in situations where previous abdominal surgery or pelvic inflammation has increased the risk of a culdoscopic accident.

We have no intention of minimizing the role of culdoscopy. Rather, we wish to emphasize the desirability of doing first that procedure, of least risk to the patient, which can still furnish sufficient indication for laparotomy.

SUMMARY

1. Visualization of the pelvic organs by gas contrast roentgenography (gynecography) is a useful diagnostic technique.

2. The method is simple. Instruments and equipment should be readily available in the radiology and supply departments of any hospital.

3. Using nitrous oxide gas, no fatalities have been reported. Morbidity is small in incidence and trivial in extent.

4. The method of patient preparation, equipment operation, roentgenographic technique and film interpretation, as well as the problems encountered, are described.

5. Several clinical problems are presented and gynecograms are illustrated.

6. The relative roles of gynecography and culdoscopy are briefly discussed.

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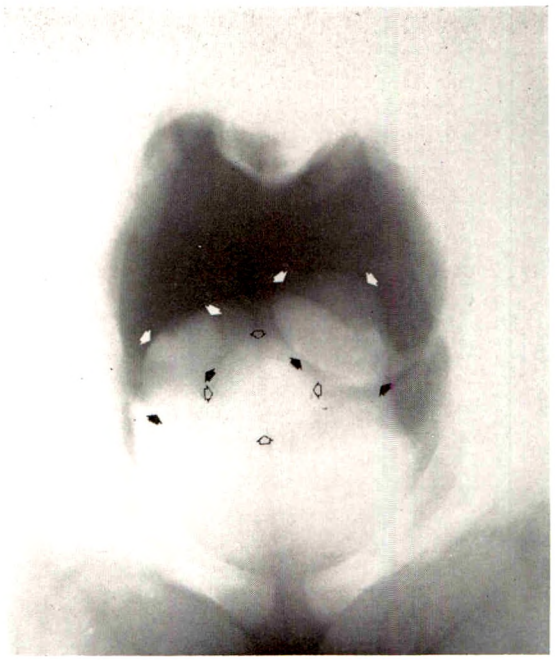


FIG. 17. (31872). Gynecogram shows ovarian enlargement in a thirty-two month old girl with precocious development and menarche at the age of eleven months. Note the ovaries (thick arrows) and uterus (outlined arrows) superimposed upon the partially filled urinary bladder.

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VOL. 86, NO. 5

BREAST ROENTGENOLOGY*

HISTORICAL REVIEW

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A REVIEW of the historical development of breast roentgenology is presented so that the experienced roentgenologist might obtain a better orientation to a roentgenographic discipline of great value in the detection of early cancer as well as other diseases of the breast.

In this country, roentgenology of the breast gained recognition in the 1950's as a useful diagnostic procedure. Many radiologists, however, still classified the examination as a special procedure, if not a technical ordeal, and many surgeons and practitioners were only vaguely aware that such an examination could be performed. Requests were few and when examinations were performed they were done often in a perfunctory manner. Most radiologists were unfamiliar with the appearance of normal breasts and, when presented with a diseased breast, were hesitant to interpret even the most clear-cut evidence of disease.

This brief review will point out some of the notable achievements as well as the many serious failures of early investigations. It will also serve to indicate areas still needing investigation, so that others may be encouraged to exploit this field to its full potentialities. Those interested in an exhaustive bibliography are urged to consult the comprehensive review published by Professor J. Von Ronnen[35] of the University of Leyden.

In 1913, a German surgeon, Salomon,[30] was the first to take roentgen-ray "pictures" of the breast. He used excised breasts, since his primary concern was to study the extent and mode of spread of mammary cancer in order that a more adequate biopsy specimen could be removed at the time of surgery. His observations of 3,000 mastectomy specimens correlated the roentgen findings with the gross and microscopic anatomy of the tumors. It is apparent that Salomon did not take full advantage of the implied diagnostic applications of his findings. However, the case histories and the descriptions and actual reproductions of the roentgenograms contain a wealth of interesting information which had considerable impact on subsequent investigators.

Salomon's most important observation was the recognition that a roentgenogram gave a true picture of the margins and extent of a tumor. He also recognized the differences in roentgen appearance of the most common forms of mammary cancer. He clearly differentiated the scirrhous or infiltrating type from the circumscribed or nodular form. Another common type, the duct carcinoma with punctate calcifications, was not recognized as a separate entity, although later duly categorized by another radiologist, Leborgne.[25] The characteristic roentgen appearance of these calcifications, however, is demonstrated in one of Salomon's illustrations. Since this appearance later acquired real diagnostic significance, the original caption is worth paraphrasing: at the center of a rather large infiltrating tumor there were many tiny calcific densities which stood out against the background on the tumor itself. Microscopic study traced the calcific deposits to cystically dilated spaces within a tumor growing, for the most part, intraductally.

In another remarkable case Salomon reports the first "clinically occult" breast cancer found by roentgen examination. In this case the breast had been removed because of a large palpable cyst. Histologic sections taken from the obvious lesion were reported as benign by the pathologist. On

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the roentgenogram of the specimen, two lesions could be clearly identified: a large, rounded, sharply defined cyst, and a tiny, very dense, spiculated tumor with the typical appearance of a scirrhous carcinoma. Unfortunately, the gross specimen in this case was lost or discarded before the roentgenograms became available for study, so no real confirmation could be made. Nevertheless, Salomon expands at some length on the very strong suspicion of malignancy discovered by means of the roentgen-ray picture.

For a number of years following Salomon's paper, there were no references to breast roentgenology in the literature. However, between 1924 and 1930, at least three independent groups were investigating the roentgen diagnosis of breast lesions. Priority is generally assigned to Goyanes, Gentil, and Guedes.[16] These authors present roentgenography of the breast as a new method of diagnosis, especially useful in differentiating inflammatory from neoplastic lesions. They described the positioning required for the examination and the normal image obtained, with its characteristic "planes." Although only a small number (56) of breasts were examined, the report was written to present preliminary findings and to encourage further use and development of the technique.

In addition to the work of Goyanes, Gentil, and Guedes, a "breast clinic" in Leipzig which was actively engaged in taking diagnostic roentgenograms of female breasts was described in Kleinschmidt's textbook.[23] The clinic and the taking of roentgenograms were under the general auspices of Dr. Erwin Payr. Dr. Payr contributed to many areas in surgery throughout a long research career, but he never personally published on the breast project.

Two papers were eventually published as a result of the work done in the Leipzig breast clinic. The later report, by Finsterbusch and Gross,[7] appeared in 1934. It is a case report on the unusual type of calcifications found in what we learned to recognize as secretory disease.[13] The report presents a very careful correlation of roentgen and histologic pathology as well as an attempt at biochemical analysis of the lesions.

The earlier paper by Vogel[34] is a classic in the field. Vogel's work is important for his roentgen classifications of various benign lesions and for his discussion of their differential diagnosis from carcinoma. The criteria used and the care given to his choice of illustrative material are still valid. Though considerably expanded, his observations form the basis of our present day interpretative criteria. Vogel also presented excellent advice on roentgenographic technique.

Although the above contributions were important, a greater impact on American radiologists was made by reports of Warren[36] and Frey and Warren.[8] Their technique—stereoscopic roentgenology—has merit and this area perhaps has not been sufficiently exploited. Warren also contributed some excellent descriptions of the normal gland at rest and during pregnancy. He differentiated the normal from the dysplastic gland and was amazed at the high incidence of the latter in his small series of cases. More important to our present day approach was his imaginative use of the roentgenogram to study breast changes over long intervals of time.

Other outstanding reports during this period were those by Seabold[31–33] and Reimann and Seabold[29] on the roentgen changes in the breast, especially during the normal menstrual cycle. Lockwood,[26,27] Lockwood and Stewart,[28] and Gunsett and Sichel[18] repeated descriptions of diagnostic criteria established by previous workers and defined some areas where inaccuracy could be expected. These difficult areas included microscopic carcinoma and small neoplasms in dense "cystic" breasts.

An often quoted work is a thesis by Espaillat[6] which appeared in Paris in 1933. The text is an attempt to correlate roentgen appearance with symptomatology and microscopic anatomy. It is perhaps the most ambitious attempt at a diagnostic manual in the area of breast roentgenology. This

work is disappointing, however, because of the incomplete analysis of the case material and because of the poor illustrations.

In 1938, Gershon-Cohen and Strickler[15] published an article on roentgenologic examination of the normal breast. They considered that knowledge of the normal breast at all ages and stages of activity was a prerequisite to recognizing pathologic conditions which might arise. The authors acknowledged that improvements in roentgen technique would advance the diagnosis of early neoplastic changes in the breast and endorsed enthusiastic application of the examination.

The literature of this decade (1930's) contains numerous other papers on breast roentgenology originating both in this country and abroad, but it seems to us that very little new information emerged from these publications. The usual pattern was a review of the current literature, followed by a review of various techniques. The diagnostic criteria first reported by the very earliest investigators were repeated and described against the background of experience with a small series of cases. The reports ended with the mention of limitations of the examination and the illustrations, when present, were not informative. It is not surprising at all that a number of people interested in the application of this diagnostic procedure should have become discouraged.

In a way, the initial failure of breast roentgenology is reflected in the first American report by Warren.[36] The main difficulty was the technical quality of the roentgenograms. A great deal of attention was given to positioning and to devices that would spread out the gland. An important diagnostic sign, punctate calcifications found in 30 per cent of all cancer cases, went unrecognized in series after series. The calcific deposits were not visualized on the roentgenograms or, if seen, were confused with artifacts.

A second fault can be traced more directly to Warren's first report,[36] in which he claimed an accuracy of 85 to 95 per cent in a highly selected series of cases. Such a high degree of accuracy impressed subsequent workers who became discouraged when the figures could not be duplicated in unselected series.

Between 1927 and 1931, Domínguez[3,4,5] of Uruguay and Baraldi[1] of Brazil published a series of reports on the use of pneumomammography as a means of obtaining better visualization of lesions in the breast. The technique was adopted in this country by Hicken,[19] who also resorted to injection of the lactiferous ducts and cystic cavities with radiopaque substances. The procedures were apparently intended to be used in cases where visualization could not be obtained by other means.

Raul Leborgne,[24] a student of Domínguez experimented with intraductal injections and he stressed the importance of good contrast which he obtained with very low kv., nonscreen film and good collimation. Use of this technique gave details previously not obtained.

The literature of the 1940's contains numerous references to the dangerous sequelae following the injection of some of these radiopaque substances. The first results were mastitis and abscess; and in isolated cases in which thorotrast was used, cancer developed (Brody and Cullen[2]).

Leborgne[25] in 1951 reported peculiar calcifications in about 30 per cent of mammary cancers, mainly of the intraductal type. Because these tumors occurred more frequently in dysplastic breasts, the sign provided an opportunity for the detection of neoplasms in a type of breast which had previously been the most difficult to examine, both clinically and roentgenographically. Since these tumors grew slowly and spread intraductually and since the patient often had little or no evidence of any abnormality, early discovery of neoplasms by roentgen examinations made clinicians and surgeons realize more fully the diagnostic value of the method.

In 1951 Gros and Sigrist[17] in Strasbourg published the first of many enthusiastic papers on breast roentgenography. They

confirmed the criteria and indications for roentgen examination and their experience with technique and case material parallels that of our own group, especially in the detection of early, clinically occult, unsuspected or asymptomatic tumors.

It is extremely difficult to evaluate our own work and that of our contemporaries at this early date. Our approach to the problem was to base roentgen examination of the breast on a firm anatomic basis. This approach was not new and can be traced as far back as the reports by Salomon, the Leipzig group and Warren. Confusion in terminology existing among surgeons and pathologists in the classification of benign and malignant lesions further complicated progress.

Collaboration with Helen Ingleby, initiated early in 1950, provided the opportunity for a thorough review of the various lesions found in the breast. Opacities seen on roentgenograms were compared with thick whole breast sliced sections of the corresponding specimen and later with the the microscopic material; this approach permitted recognition on the roentgenogram of shadows which had previously appeared unimportant. Observations of abnormal areas on the roentgenogram might call for a search of the surgical specimen for previously unrecognized abnormalities. In more recent years, we were able to correlate roentgen and pathologic findings with certain clinical entities, chiefly adenosis and secretory disease. Use of repeated examinations has been applied to such problems as mammary abscess, pregnancy and lactation and the mode and rate of growth of mammary cancer.[9–14,20–22]

There are still confusing aspects in roentgenology of the breast to be studied and the recent revival of interest in this field is encouraging. Technical improvements of roentgenograms and illustrations, detection of clinically unsuspected carcinomas and the early visualization of lesions for biopsy all have contributed to interest in this field. It is hoped that investigations will continue and that the uncertainties of clinical examination of the breast will be resolved by routine use of this very useful diagnostic procedure.

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THE MOTOR ACTIVITY OF THE ESOPHAGUS IN ASSOCIATION WITH ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA*

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PATIENTS who have had surgical repair of esophageal atresia, with or without a tracheoesophageal fistula, often have symptoms as a result of dysphagia, impaction of foreign bodies, and regurgitation with aspiration and subsequent pulmonary infection. These manifestations are usually encountered in the immediate postoperative period, again when solid foods are introduced into the diet, and later in life when solid food is masticated incompletely or swallowed hastily. Cinefluorographic studies of the swallowing act show that narrowing of the lumen of the esophagus at the site of the anastomosis may contribute to the symptoms, but that there is, in addition, a functional disturbance in motor activity of the esophagus of considerable importance.

MATERIAL AND METHOD

Cinefluorographic studies of the esophagus of 15 patients who had a primary anastomosis of the esophagus have been carried out since 1956. In 14 patients, the initial study was performed two to three weeks postoperatively. When subsequent studies were made, these were done at intervals of two months to three years. One patient was examined first at seven years of age and then again two years later. Five patients were examined once, 4 patients were examined twice, and 6 patients were examined three or more times. The patients were examined while prone (left posterior oblique position). A mixture of barium and water was utilized as contrast material. The exposure was made on 16 mm. movie film (Kodak Linagraph Shellburst) at 24 or 32 f/sec. during and after swallowing this material. A 16 mm. Bell & Howell camera, with a 0.95, 25 mm. lens mounted on a 5 inch image intensifier,* was utilized to record the swallowing act.

DISCUSSION

Cinefluorography of normal infants and children reveals a pattern of deglutition comparable to that described as occurring in adults.[2] Deglutition may be divided into three stages. The first stage is voluntary and is concerned with the propulsion of the bolus of liquid or solid material into the pharynx. The presence of the bolus in the pharynx stimulates the reflexes responsible for the second and third stages, which are involuntary. The second stage is characterized by closure of the oral cavity, nasopharynx and larynx; contraction of the pharyngeal constrictors (initiation of the primary peristaltic wave); and relaxation of the cricopharyngeus muscle. The third stage is the continuation of the primary peristaltic wave down the esophagus and the relaxation of the esophagogastric junction. The passage of liquid is as a solid bolus when the patient is supine; when the patient is erect, the liquid precedes the primary peristaltic wave and is held up at the lower end of the esophagus until the wave reaches this area. A succession of swallows of liquid will inhibit the primary peristaltic wave. Secondary waves in the vicinity of the bolus may be initiated by local distention of the esophagus. Reverse peristalsis does not occur in the esophagus,

* Manufactured by North American Philips Company, Inc.

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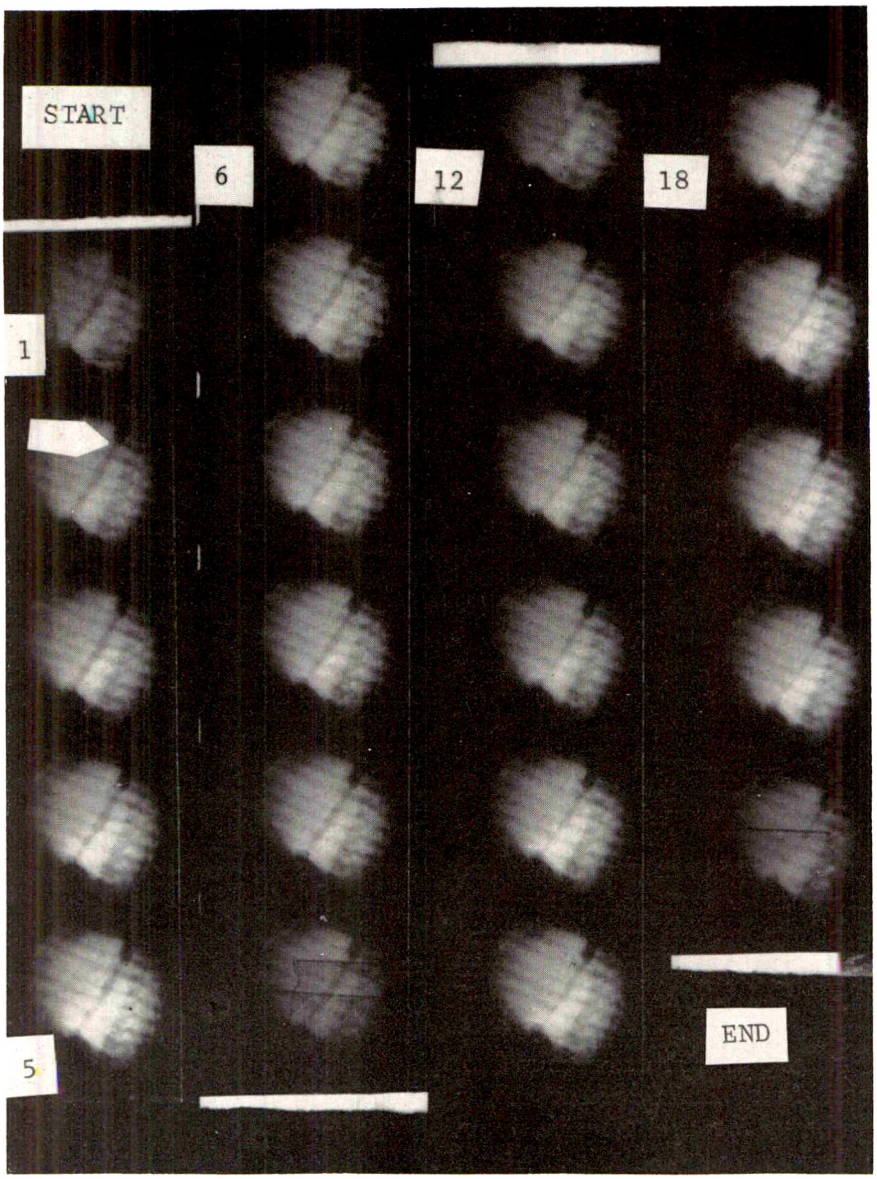


FIG. 1. A selected cine sequence of a patient who had surgical repair of esophageal atresia and tracheoesophageal fistula (left anterior oblique position). The arrow points to the line of anastomosis. Contrast material remains in the esophagus after feeding. The sequence demonstrates contraction of the lower esophagus with retrograde flow of barium into the esophagus above the line of anastomosis.

but a reverse flow of esophageal contents may be caused by nonpropulsive contractions which spread upward.

Patients who have had repair of esophageal atresia, with or without tracheoesophageal fistula, do not show coordinated activity. The primary peristaltic wave is initiated in the pharynx, but does not progress along the length of the esophagus. In many instances, it becomes dissipated above the line of anastomosis so that the contrast material remains in this area until a mass contraction occurs. Then, some of the contrast medium may pass in a retrograde manner into the pharynx, but the bulk usually goes past the line of anastomosis into the lower esophagus. Although the initial impression in these instances

may be that of an organic obstruction at the line of anastomosis, it seems probable that, at least a considerable portion of the obstruction is functional, being dependent upon the disturbed motor activity. Contrast material in the esophagus below the line of anastomosis, if of an amount that does not distend the esophagus, may remain in the esophagus for many minutes until it flows downward. If of an amount to result in distention of the esophagus, secondary contractions may occur that are either localized to the point of maximal distention or are more diffuse and involve most of the lower esophagus. These contractions result in both antegrade and retrograde flow of the contrast material. In several patients, the retrograde flow was sufficient to enter the pharynx and spill over into the larynx and airway. In some patients, the esophagogastric junction was competent; in others, there was free flow from the stomach into the esophagus with crying and subsequent increase in intra-abdominal pressure (Fig. 1).

Not in all patients was the extreme form of the abnormal motor activity apparent, and symptoms were not present in all patients. In all the postoperative patients examined cinefluorographically, however, there was some degree of incoordination of primary peristalsis, particularly below the line of anastomosis. Haight[1] has referred to this abnormality in 5 patients, six to eight and one-half years of age, examined by means of a rapid cassette changer. In one of our patients, seven years of age, the mother stated that the child would regurgitate if he ate too rapidly or masticated insufficiently. He demonstrated deficient motor activity below the line of anastomosis and, at times, retrograde flow in the esophagus but not into the pharynx.

The motor activity in the esophagus in these patients is not unlike that described after the administration of banthine (methantheline), an anticholinergic agent.[3] Thus, one is led to speculate that the abnormality is secondary to interruption of the vagal fibers to the esophagus at the time of surgical intervention. To date, however, it has not been possible for us to correlate the amount of operative dissection with the postoperative activity of the esophagus. We have had the opportunity, moreover, of examining pre-operatively one newborn infant with a tracheoesophageal fistula and a stenosis of the esophagus. There was deficient peristalsis below the fistula and below the area of stenosis with reflux of contents from the lower esophagus through the fistula and into the trachea, as well as from the stomach into the esophagus and into the trachea. Therefore, this abnormality in motor activity may well be an inherent defect in vagal innervation that is compounded by the surgical procedure. Because of the latter observation (gastroesophageal reflux) patients with esophageal atresia and tracheoesophageal fistula are placed in a semi-erect position before and after surgery. This position, pre-operatively, may minimize the retrograde flow of gastric juice (which is particularly acid during the first twenty-four hours of life) through the fistula and lessen the degree of pulmonary involvement. After surgical repair, the semi-erect position facilitates the passage of food through the esophagus and into the stomach.

SUMMARY

Cinefluorographic studies of 15 patients operated upon for esophageal atresia, with or without tracheoesophageal fistula, have demonstrated disturbed motor activity of the esophagus. This, when marked, may lead to recurrent aspiration pneumonia and favor the incarceration of foreign bodies in the esophagus. Its observation, pre-operatively, in a patient with tracheoesophageal fistula and esophageal stenosis, raises the question of an inherent vagal deficiency. The semi-erect position is preferred for the patient awaiting surgery, as well as for the postoperative patient.

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ABERRANT INSERTION OF A PULMONARY VEIN INTO THE LEFT ATRIUM SIMULATING AN INTRINSIC LESION OF THE ESOPHAGUS

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AMONG the many congenital malformations of the heart and great vessels, anomalous drainage of the pulmonary veins into the systemic venous circulation is a well-recognized entity. If the anomalous drainage affects the total pulmonary blood flow, life is possible only if there is an associated intracardiac shunt, commonly an atrial septal defect. Partial drainage of one lung or of an individual pulmonary vein into the right auricle may be present as an isolated finding. With the development of cardiac catheterization and angiocardiography, anomalous pulmonary venous drainage has become a relatively common diagnosis.

Other rare abnormalities of the pulmonary veins have been described which primarily concern variations in the total number of veins emptying into the left atrium. This is generally ascribed to the degree of resorption into the atrial wall of the original common pulmonary venous trunk into which the individual pulmonary vessels converge. It is conceivable that variations in the degree of resorption might not only affect the number of pulmonary veins but also their place of insertion into the atrial wall. The result would be an "aberrant" venous insertion.

The authors define aberrant venous return as a condition in which a pulmonary vein inserts into its normal chamber, the left atrium, but the course of the vein varies from the usual pattern. Anomalous venous return represents a deviation from the natural order of embryologic development in which the pulmonary vein inserts outside of the left atrial chamber, compromising the physiologic function.

The following report concerns an aberrant insertion of a left pulmonary vein into the left atrium which, by its position, produced unusual clinical symptoms and roentgen findings.

REPORT OF A CASE

A forty-nine year old white female was first admitted to Lebanon Hospital in October, 1958, with a five month history of precordial pain, substernal in character, radiating to the back and left side. This was associated with episodes of dysphagia, retching, vomiting and, occasionally, syncope.

The past history revealed numerous hospital admissions, including one in January, 1939, for acute epigastric pain associated with tarry stools. Thorough examination at that time failed to demonstrate a causative lesion. In recent years she had been treated for diabetes mellitus, arteriosclerotic heart disease with mild coronary insufficiency and a persistent tachycardia of 120–130 per minute. Further history, after admission, disclosed that the symptoms of dysphagia had been present for many years. She described frequent episodes consisting of a sudden onset of dysphagia, followed by tachycardia, dyspnea, vertigo and incipient syncope. These attacks sometimes occurred during sleep and particularly when she was on her left side. The patient had developed a persistent nonproductive cough a few months prior to the first admission, with one equivocal episode of hemoptysis following a bout of coughing. An intensification of the intermittent dysphagia accompanied these symptoms. Just prior to this admission, the patient was awakened from sleep by severe precordial pressure, dysphagia, retching and collapse, which led to the initial investigation in October, 1958.

Physical examination, on admission, disclosed the blood pressure to be 100/60, with a regular sinus rhythm and a tachycardia of 120

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per minute. A Grade II systolic murmur was heard over the aortic and pulmonic areas with an accentuation of the second pulmonic sound. A mild exophthalmos was present; the thyroid was not palpable. The remainder of the physical examination was within normal limits. Laboratory findings revealed the blood chemistry, blood count and sedimentation rate to be within physiologically normal limits. The electrocardiograms did not point to an acute cardiac episode, but were consistent with arteriosclerotic heart disease and coronary insufficiency. Roentgenograms of the chest were within normal limits. Radioactive iodine uptake studies were normal.

The patient's stay in the hospital was uneventful and she was discharged, at her request, ten days after admission. During the following two months the patient experienced intermittent episodes of dysphagia and retching, which were not severe. She was maintained on digitalis and oral diuretics because of early signs of congestive cardiac failure. At the beginning of December, 1958, the patient developed bouts of right upper quadrant pain, at intervals of two to three days, which increased in severity. These appeared to be unrelated to her previous complaints of dyspnea, dysphagia and the cardiovascular symptomatology, and led to the second admission in December, 1958.

Physical examination, laboratory and electrocardiographic findings were essentially unchanged. The cardiac symptoms were easily controlled with bed rest and medication. Roentgen studies were requested for possible hiatus hernia, peptic ulceration or gallbladder pathology, since the clinical picture suggested a subdiaphragmatic cause for the symptoms.

The initial gastrointestinal series disclosed a large impression upon the anterior wall of the esophagus in the region of the left atrium, with a moderate delay in the passage of the contrast medium at this point. The remainder of the examination revealed the esophagus, stomach and duodenum to be within normal limits. Small bowel examination appeared normal. A repeat examination of the esophageal lesion primarily suggested an intrinsic lesion of the esophagus, intramural in type, due to the overhanging edge on the inferior margin of the lesion (Fig. 2, *A* and *B*). The appearance of the lesion and the clinical evaluation did not suggest simple enlargement of the left auricle. Chest roentgenograms disclosed no abnormality. On esophagoscopy, the esophagoscope passed into the stomach with ease and revealed a normal esophageal mucosa with no evidence of displacement or of external pressure. Laminagraphy of the posterior mediastinal area, with a barium filled esophagus, revealed intimate association of the left auricular appendage with the esophageal defect. The possibility of a localized lesion of the left atrium or appendage was suggested as the probable causative factor.

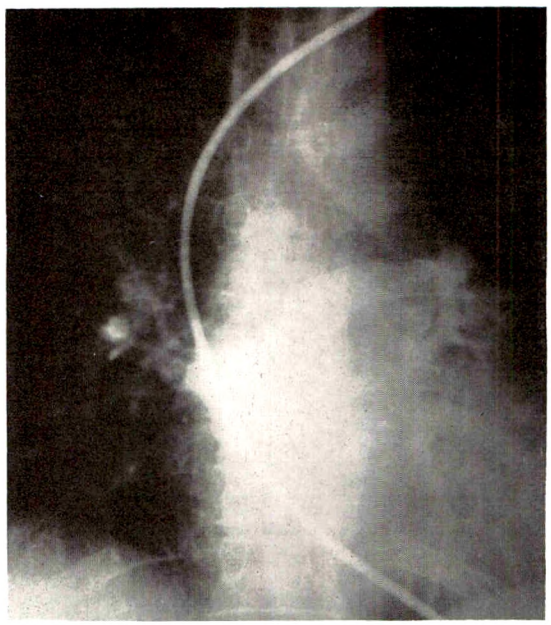


FIG. 1. Anteroposterior angiocardiogram showing a left pulmonary vein entering the superior aspect of the left atrium somewhat more medially than is usually seen.

Angiocardiography was performed in the frontal and lateral projections using 30 cc. of 90 per cent hypaque injected into the right ventricle through a No. 8 Lehman catheter. The right ventricle appeared minimally dilated. The pulmonary arteries revealed a normal distribution and normal cycle of filling and emptying. Figure 1, taken anteroposteriorly at approximately four seconds after the commencement of injection, shows one of the left pulmonary veins inserting into the superior aspect of the left atrium somewhat more medially than is usually seen. The vein appears dilated and larger in caliber than any of the other visualized pulmonary veins. To study the possibly aberrant course of this vein, angiocardiography was performed in the lateral projection with a barium filled esophagus. Figure 2*A*, taken approximately one second after the commencement of injection, reveals excellent visualization of the right ventricle and right

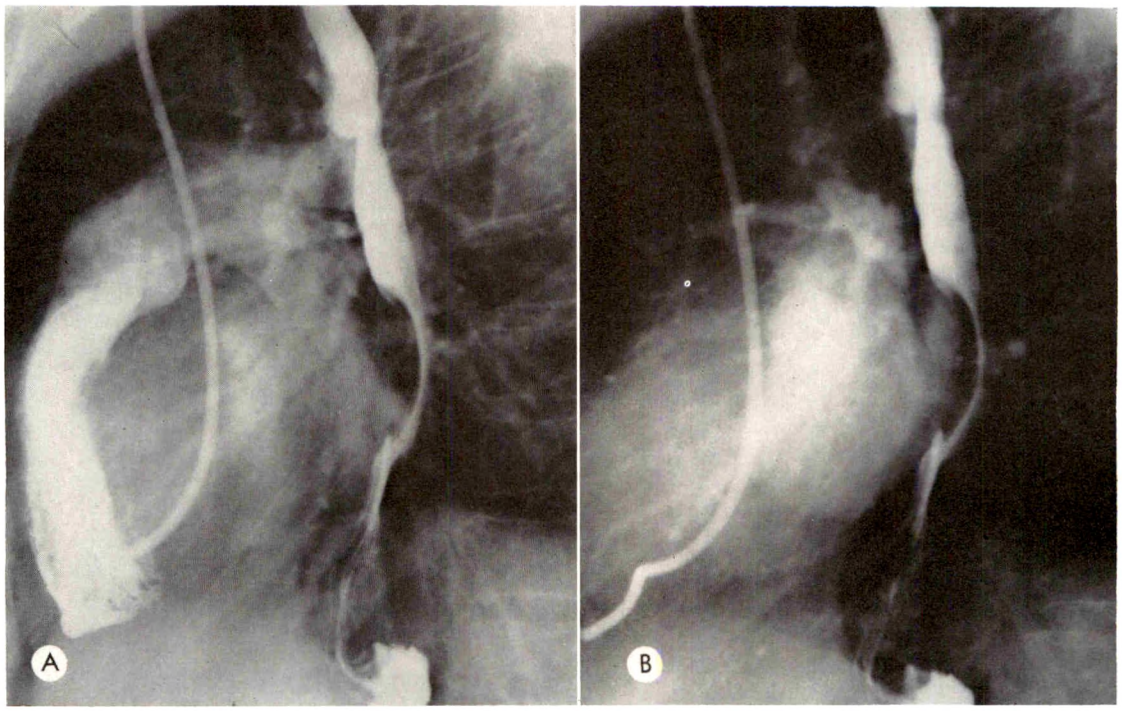


FIG. 2. Lateral angiocardiograms at (*A*) one second and (*B*) four seconds after injection of the contrast medium to show the aberrant course of the left pulmonary vein.

ventricular outflow tract. There is no contrast medium in the area of the esophageal defect. Figure 2*B*, four seconds after the commencement of injection, demonstrates the large left pulmonary vein to be passing over the superior aspect of the left atrium and inserting into the posterior aspect at approximately the midpoint of the chamber. The vein occupies the entire defect in the esophagus and thus can be assumed to be the cause of the defect.

It was felt that this finding satisfactorily explained the symptomatology and the defect noted on the esophageal study. Surgery was not advised to correct this condition. The reason for the attacks of right upper quadrant pain was provided by the results of intravenous cholangiography, which disclosed a stone impacted in the cystic duct. Cholecystectomy relieved these symptoms. Following surgery, fluoroscopic and roentgenographic examinations of the esophagus did not disclose any change in the extent or appearance of the indentation caused by the aberrant insertion of a left pulmonary vein into the left atrium.

The symptoms which initiated the investigation still recur intermittently, but are not incapacitating. Knowledge of the causative factor has relieved the patient's anxiety.

DISCUSSION

Whereas the literature contains numerous reports of anomalous pulmonary venous drainage (complete or partial) into the right atrium or its tributaries, abnormal insertion of a pulmonary vein into the left atrium, with normal drainage, has not been recognized as a clinical entity.

The seemingly unrelated variations that occur in the pulmonary venous drainage have been well understood from the study of the embryology of the pulmonary vascular tree.[2] Similarly, variations in the number of pulmonary veins draining into the left auricle are readily explained if we remember that the pulmonary venous plexus is composed of individual veins which drain the various lobes of the lung buds and which then form a common pulmonary vein entering the left atrium dorsally. Usually, this main pulmonary vein and its branches are incorporated into the dorsal aspect of the left atrium during the formation of this chamber, so that two branches open into the left atrium on either

side. If the common pulmonary vein is incorporated to a lesser degree, single instead of paired vessels may be encountered, and vice versa. Thus Brantigan[1] describes seven varieties of venous insertion. Although occasionally seen at the operating table, this abnormality has, to our knowledge, not been associated with clinical symptoms.

The abnormality visualized in our patient differs from those described by Brantigan as there occurred a cross-over of the left pulmonary vein, which, instead of entering the left atrium on the left, entered it to the right of the midline. As in abnormalities of the aortic arch, such as an arteria lusoria, the importance of this anomaly depends upon whether it produces symptoms. While with an arterial lesion the symptoms are unquestionably those of pressure by the artery on neighboring structures, the symptoms produced in the case of a "vena lusoria" may not only be those of pressure by the vein on neighboring structures but also those of pressure by the neighboring structures on the vein. Due to the low pulmonary venous pressure, the latter condition would appear to be more likely giving rise to symptoms of pulmonary congestion.

The esophageal studies in our patient were performed because of a presenting symptom of dysphagia. The roentgenologic finding on barium swallow was that of an esophageal defect which simulated an intramural, extramucosal lesion of the esophagus. The differential diagnosis was between such an esophageal lesion, bizarre enlargement of the left atrium, tumor of the pericardium and unusual enlargement of the esophageal lymph nodes. The negative esophagoscopy suggested that the defect was produced by extrinsic pressure which could be relieved by pressure of the esophagoscope and this, in turn, suggested a vascular anomaly.

It is surprising that the presenting symptom, dysphagia, was caused by the aberrant course of the pulmonary vein. As stated above, the low pressure pulmonary system would appear more likely to bear the brunt of the pressure with resultant pulmonary congestion. However, the defect seen on barium swallow and which could not be visualized on esophagoscopy was conclusively proved by angiocardiography to be a pulmonary vein crossing in front of the esophagus.

The authors have knowledge of 1 case with similar findings which was operated upon in a New York hospital for a probable leiomyoma of the esophagus. At surgery, an aberrant pulmonary vein causing the esophageal defect was found.

Obviously, this diagnosis can only be made if the opacification of the vein can be seen by angiocardiography. Therefore, this procedure should be considered when the clinician is faced with an unusual defect of the esophagus in the region of the left atrium and a negative esophagoscopy.

SUMMARY

1. Variants in the insertion of pulmonary veins into the left atrium can be easily explained on an embryologic basis.

2. The possibility of such an aberrant insertion causing symptoms of dysphagia is illustrated by the case reported.

3. Since anomalous drainage of pulmonary veins into the systemic venous circulation is known as anomalous pulmonary venous return, the variant described above has been terned "aberrant insertion of the pulmonary vein into the left atrium." It is felt that this is probably a frequent occurrence, although causing symptoms rather rarely.

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LIGNIBEZOAR

REPORT OF A CASE

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BEZOARS have been the source of much interest for many centuries. Indeed, in the 1500's, and possibly even before, an animal bezoar was highly valued for the great powers that it was thought to contain. It was believed that, if the owner were to wear it as a charm or to ingest a particle of it, he would be protected from or cured of a wide variety of maladies, such as epilepsy, plague, headache, dysentery, leprosy, and vertigo. In addition, it would neutralize any poison and would be an effective agent against hemorrhage. In return for one of these wonderful stones, great sums of money changed hands. They became more valuable than gold, silver, and precious jewels.

Man's only interest in bezoars was as a source of miraculous remedy until the late 1700's at which time the first human bezoar was found. Over the years since then, man's superstitious interest in bezoars has given way to an interest in bezoars as a medical curiosity. Though there are about 400 cases reported in the literature, the majority of authors still considers them a rarity.

The definite diagnosis of a bezoar on the basis of history and physical examination alone is unusual and the best that can be hoped for is its inclusion in the differential diagnosis. The patient will rarely volunteer the information that he has eaten hair, persimmons, or other substances related to bezoar formation and it is unusual for the clinician to ask such questions. The symptoms of anorexia, epigastric distress, pain or tenderness, nausea, vomiting, abdominal mass, weakness, weight loss, constipation, and diarrhea, alone or in combination, common to bezoars, are certainly not pathognomonic and could well point to any one of many gastrointestinal disorders. If intestinal obstruction, gastric ulcer (which is usually on the lesser curvature), or perforation of an ulcer should occur as a result of the bezoar, the patient will present with the usual symptoms of that particular gastrointestinal complication.

Laboratory studies may help to point the way to a correct diagnosis. The majority of cases are accompanied by a mild leukocytosis and a slight secondary anemia. In the case of a trichobezoar, gastric analysis frequently reveals low acidity, while normal or high acidity is usually found in cases of phytobezoars. In addition, bits of the component material may be obtained with the specimens for gastric analysis. Also, stool examination may reveal particles of the offending substance.

The roentgenographic examination will usually reveal the correct diagnosis. It can be said that the characteristic roentgen findings, by both roentgenography and fluoroscopy, are pathognomonic. At the fluoroscopic examination, the ingested barium meal will be seen to outline the stomach walls leaving a radiolucent filling defect within the lumen of the stomach. At the same time, it may be noted that the stomach is distended. As more of the barium meal passes into the stomach, the general outline of the filling defect remains but it will begin to take on a striated or mottled appearance as the barium fills the small spaces between the particles of matter making up the bezoar. The general outline of the filling defect will usually match that of the stomach itself. The mass is frequently movable on palpation and, when the stomach is filled with barium, it may be pushed toward the gastric fundus so that a portion of this striated or mottled mass will protrude into the gastric air bubble above the air-fluid level. The roentgenograms will confirm the fluoroscopic findings. It is frequently helpful to obtain a roentgenogram of the abdomen several hours after the

initial examination, when the stomach has emptied the barium contents, since it will frequently reveal in the region of the stomach a mass which has a striated or mottled appearance due to barium temporarily trapped in crevices between the consituent particles of the bezoar.

Many fine articles concerning bezoars can be found in the literature. Rather than to attempt to repeat what has been so adequately written by others, the foregoing was designed as a brief summary of bezoars in general. For greater detail, the reader is referred to the reports of Thorington,[2] DeBakey and Ochsner,[1] Tondreau and Kirklin,[3] and others who have contributed to our knowledge of bezoars through the medical literature. The primary purpose of this report is to present a case history of an unusual type of bezoar, one consisting of wooden splinters.

REPORT OF A CASE

The patient was a well developed, well nourished eighteen month old white male child. The parents noted him chewing on parts of the crib railing. Eventually, about ½ inch of the wood had been removed most of the way around the crib with no evidence of the pieces to be found. Two or three days after this wood chewing was first noticed, the patient began to pass wooden splinters in his stools. At this point, the crib railing was covered with tape to prevent further chewing. He continued to pass 3 to 5 loose stools per day, all with considerable mucus and bits of wood. On one occasion he vomited pieces of wood up to 2½ inches long. During ths time, he had continued to eat well. The parents stated that the child had no apparent abdominal pain but he did cry when moving his bowels. The patient was seen by the family physician who suggested that he be admitted to the hospital to determine the amount of wood remaining in his gastrointestinal tract.

The child was admitted to the Robert Packer Hospital in Sayre, Pennsylvania, on March 25, 1960, approximately three weeks after he was first noticed chewing on his crib. He continued to pass splinters in his stools (Fig. 1) but had no more episodes of vomiting after the original single occasion.

The system review was negative and it was

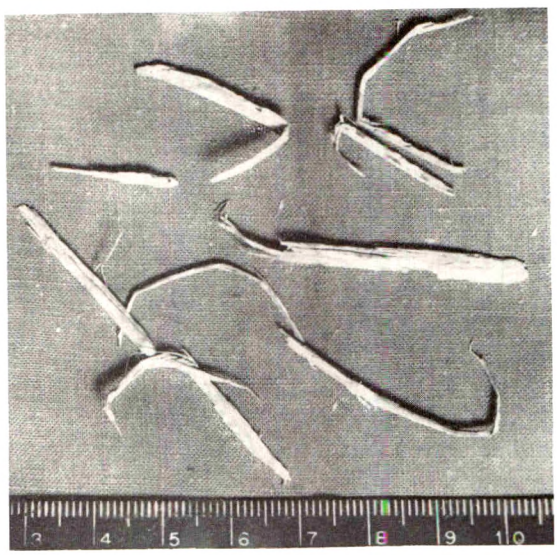


FIG. 1. A few of the wooden splinters found in the patient's stool. The scale is in centimeters.

determined that he had been gaining weight, although slowly. He had been hospitalized at Robert Packer Hospital in November, 1959 for bronchopneumonia which had responded well to treatment. There were no known allergies. He was eating table foods and taking vitamins.

The physical examination revealed a normal, alert, cooperative child weighing 31 pounds. No abnormalities were found.

A blood count obtained on the day of admission reported 8.9 gm. of hemoglobin, hematocrit 31 per cent and a white blood cell count of 6,650 with a differential of 44 per cent neutrophils and 56 per cent lymphocytes.

Also on the day of admission, a gastroduodenal examination was requested of the Radiology Department. At fluoroscopy, after ingestion of a barium mixture, a rather large filling defect was noted within the lumen of the stomach; it was roughly triangular in shape with the apex projecting into the gastric antrum. The mass was freely movable and the fluoroscopist gained the impression that it floated on the ingested barium-water mixture. The walls of the stomach appeared normal and barium was seen to pass freely from the stomach into the duodenum. The duodenal bulb appeared to be within normal limits. The spot roentgenograms revealed a negative filling defect within the gastric lumen (Fig. 2). This defect appeared to contain linear striations of increased density apparently due to the ingested barium. A roentgenogram obtained one



FIG. 2. Spot roentgenogram, obtained during the fluoroscopic examination, showing the stomach filled with barium and the bezoar represented by a mottled, striated negative filling defect.

hour after the initial examination revealed the barium meal passing freely through a normal small intestine. Another roentgenogram taken four hours after the barium had been ingested

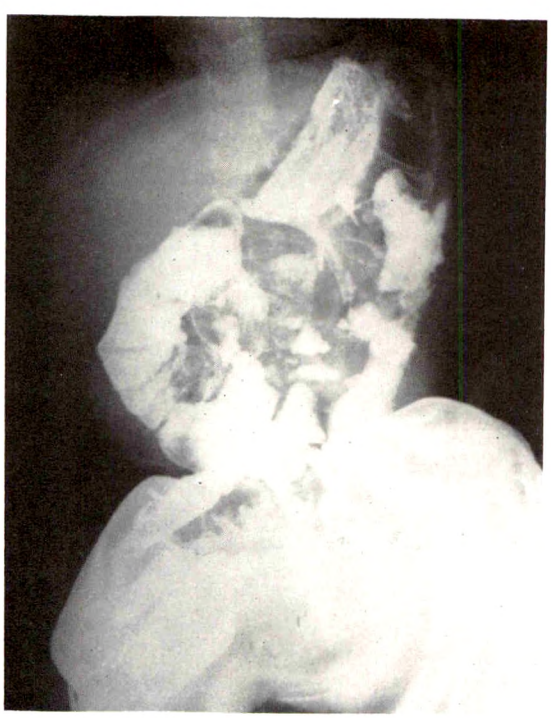


FIG. 3. Roentgenogram obtained four hours after ingestion of the barium meal showing the barium impregnated bezoar in the stomach and the barium meal in the large and small intestine.



FIG. 4. The bezoar, consisting of wooden splinters, which was removed from the patient's stomach at surgery. The scale is in centimeters.

revealed a barium coated foreign body within the stomach, with no residual free barium (Fig. 3). The roentgen diagnosis was reported as a foreign body within the stomach having the appearance of a bezoar.

A single scout roentgenogram of the abdomen was obtained three days after the initial examination; it once again showed the barium impregnated mass in the region of the stomach. It appeared to be of the same size as originally noted. A period of forty-eight hours passed during which no splinters of wood were found in the stool so it was decided that the bezoar should be removed surgically.

On March 29, a gastrotomy was performed. At operation, a large mass was felt in the stomach and, after opening the stomach, a large ovoid concretion composed of numerous wooden splinters cemented together by thick mucoid material was removed (Fig. 4). The mass measured 9.5 cm. in length by 3.5 cm. in width. The wooden splinters averaged 6 to 9 cm. in length. A thorough search was made for other splinters, but none were found, and the stomach was closed.

The patient did well postoperatively and no complications were encountered. He was discharged on the ninth postoperative day, April 7, 1960.

DISCUSSION

Bezoars have been divided into four categories on the basis of their constituent materials. Trichobezoars are those composed of hair. They range from human hair through animal hair to string and thread. Phytobezoars are composed of various food materials of plant origin. They may consist

of stems, fibers, leaves, roots, and seeds. The most common in this category are persimmon bezoars. Trichophytobezoars are those composed of a combination of the materials in the above two categories. The fourth category includes miscellaneous bezoars and concretions which have been reported as consisting of asphalt, shellac, sand, and other substances.

The bezoar described in this presentation would most likely be classified in the fourth category as a miscellaneous bezoar. True, it is of plant origin but it certainly is not a food substance and, therefore, not a true phytobezoar. It is suggested that bezoars of this nature might be termed lignibezoars.

SUMMARY

A brief summary has been presented of the history, symptoms, and laboratory and roentgen findings of bezoars. A case history has been reported of an unusual type of bezoar consisting of wooden splinters with the suggestion that it might be termed a lignibezoar.

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PRIMARY RHABDOMYOSARCOMA OF THE STOMACH AND ESOPHAGUS*

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PRIMARY rhabdomyosarcoma of the upper gastrointestinal tract is a rare tumor. Stout and Lattes[6] reviewed 4 cases of rhabdomyosarcoma primary in the esophagus, and Stout[7] has seen 2 cases of rhabdomyosarcoma involving the stomach. Geschickter,[2] Gordon-Taylor,[3] and Pack and Ariel[5] in their extensive reviews of striated muscle tumors do not include any cases in which the esophagus or stomach was the organ of primary involvement.

The roentgenologic, radiotherapeutic, surgical and pathologic findings in 2 cases of rhabdomyosarcoma that involved the stomach and upper esophagus respectively form the basis of this report.

Rhabdomyosarcomas occur in both sexes equally and at any age. Trauma does not appear to be a causative factor. Although the exact etiology is unknown, the congenital theory appears to be most tenable. Geschickter[2] has pointed out that within the first month of embryonic life the primitive digestive tube is partially invested with a sheet of mesoderm from which a part of the body's skeletal musculature is derived. Also, mature striated muscle cells are completely differentiated end products and are unable to undergo cell division. The growth characteristics of these tumors are extremely variable.[3]

Rhabdomyosarcomas tend to metastasize quite early to the lungs via the blood stream. They may, less commonly, disseminate by way of the lymphatic system. Pack and Ariel[5] who show a 33 per cent five-year cure rate in their series, feel that surgery is the treatment of choice; however, the judicious use of radiation therapy has a definite place in the over-all management of the patient with this lesion.

REPORT OF CASES

CASE 1. A three year old Negro male was seen at Henry Ford Hospital with a six month history of painless swelling in the right neck. Physical examination was completely negative except for a 4×6 cm. freely movable, spherical, cystic mass located in the anterior triangle of the neck.

Surgical exploration of the neck on June 13, 1960 disclosed a tumor which did not appear to arise from, nor have any connection with, the surrounding musculature. It was completely excised, and the pathologic interpretation of the frozen sections was "cervical lymph node, almost completely replaced by tumor."

Subsequent paraffin sections of the tumor tissues stained with hematoxylin and eosin showed a highly cellular tumor with a scanty fibrous tissue stroma. There were clusters, sheets and clumps of both, small round cells with minimal cytoplasm and larger spindle shaped cells, some of which were in an alveolar pattern. These latter cells showed polar elongation of the cytoplasm into homogeneous pink processes in which no fibrils or striations could be definitely identified. Imprint preparations showed fairly uniformly distributed chromatin particles in the nuclei. Of special interest was the identification of giant, intensely pink, glassy appearing nucleoli. The final diagnosis was rhabdomyosarcoma partially replacing a lymph node.

Numerous physical, laboratory, and roentgen examinations did not demonstrate the primary tumor site. The child was discharged on June 19, 1960, to be followed in the out-patient clinic.

One month later he was re-admitted with a two week history of anorexia, intermittent vomiting of yellow bile-like material and a four pound weight loss. There was no history of hematemesis or melena.

Physical examination at this time revealed a firm, nontender, well circumscribed abdominal

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mass projecting from beneath the left costal margin. Bowel sounds were normal, and the abdomen was not distended. The chest was clear. Laboratory studies were noncontributory. The child developed symptoms of increasing high intestinal obstruction. Roentgen studies of the abdomen (Fig. 1), urinary system (Fig. 2), and upper gastrointestinal tract (Fig. 3) were obtained.

Because of the roentgen demonstration of a large gastric tumor, a laparotomy was performed on July 27, 1960. A huge mass was immediately encountered arising from and involving the upper two-thirds of the stomach. The gastric mass was contiguous with large indurated lymph nodes located in the pyloric, celiac and porta hepatis areas. The pylorus itself was infiltrated and partially obstructed. Since curative surgery was not thought possible, a gastrojejunostomy was done and multiple biopsies were taken.

The patient's immediate postoperative course was satisfactory. Because of the large mass encroaching on the lumen of the proximal stomach, further obstruction was anticipated. Radiation therapy was therefore initiated in an effort to reduce the tumor mass. A minimum tumor dose of 4,500 r was planned, and, if at the end of this time the patient was tolerating the radiation satisfactorily, the tumor dose would be carried to 6,000 r. Cobalt 60 was used with a daily tumor increment of 200 r. Unfortunately, during the next two weeks the

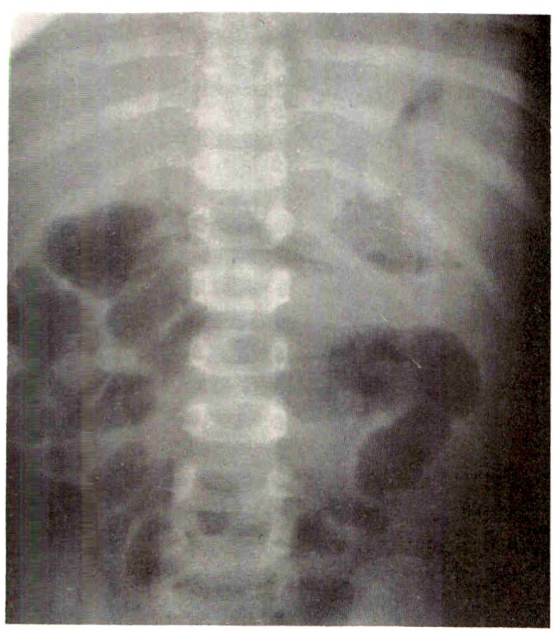


FIG. 1. Case 1. Supine roentgenogram of abdomen demonstrating a large homogeneous soft tissue density in the left upper abdomen and deformity of the gastric air bubble.

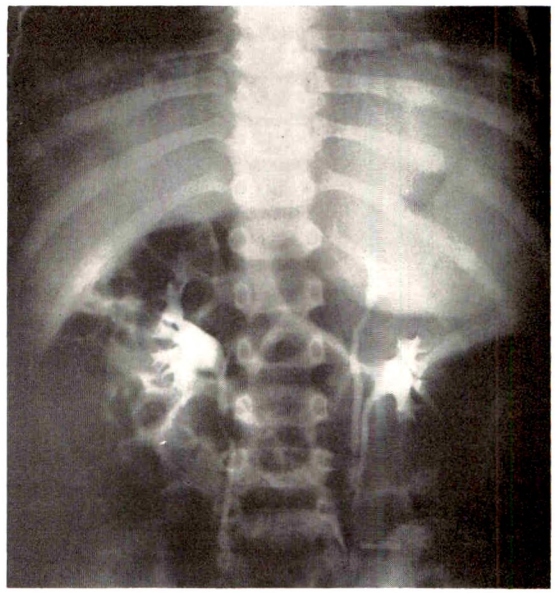


FIG. 2. Case 1. An excretory urogram shows normal renal outlines, position and collecting systems. The mass in the left upper quadrant is sharply outlined.

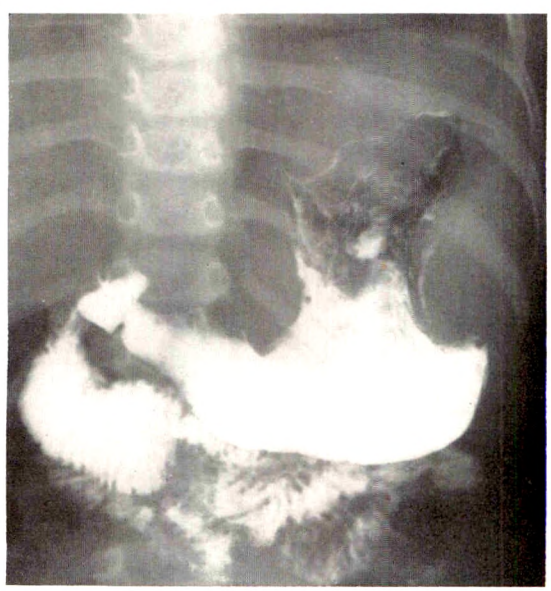


FIG. 3. Case 1. A roentgenogram of the stomach demonstrates a large gastric mass producing a filling defect in the fundus and body of the stomach. There is generalized mucosal destruction.

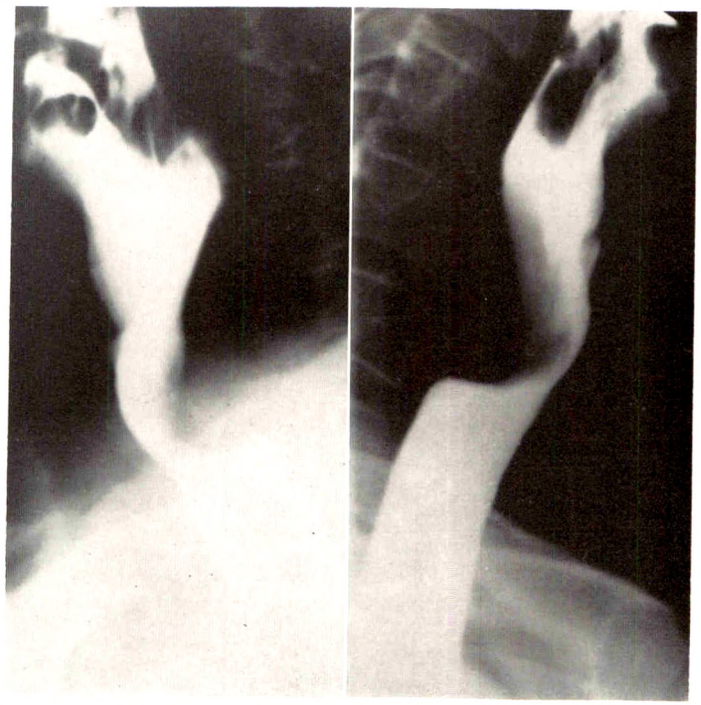


Fig. 4. Case 11. Esophagrams show a smooth, intramural defect in the posterior cervical esophagus.

patient began to accumulate ascites and developed urinary retention. Therapy had to be discontinued on August 18, 1960 after a tumor dose of 2,200 r had been delivered. The child expired ten days later.

Significant autopsy findings were limited to the abdomen. The entire stomach was involved by a huge tumor mass which extended to the second portion of the duodenum, the left lobe of the liver, and the undersurface of the left hemidiaphragm. In addition, there was direct extension of tumor into the pancreas. Metastatic disease was not found. Microscopic examination of the tumor tissues revealed a pattern entirely similar to that seen in the cervical lymph node. There was no histologic evidence of any nuclear or cellular change that could be attributed to radiation.

Comment. Malignant tumors of the stomach are very unusual in young children.[1] McNeer[4] in reviewing the world literature found 19 cases of gastric cancer in the age period from birth to fifteen years. The sites of malignancy in children differ from those in adults, and, although no part of the body is exempt, 80 per cent of all malignant tumors in young children occur in the adrenals, kidneys, eyes, blood, brain or bones.[8] There is little correlation between the histologic characteristics of a particular tumor and its biologic behavior.

There was a time lapse of six weeks from the initial physical examination and cervical lymph node excision to the day of abdominal exploration. In this time the large epigastric mass became apparent. Such rapid enlargement would be typical of the "hurricane" growth described by Gordon-Taylor.[3] The factor, or factors stimulating such sudden and rapid tumor growth remain unknown.

The first and only known distant metastasis in this case was to a cervical lymph node. There was also extensive spread of the tumor to the celiac and portal lymph node structures at the time of laparotomy and autopsy. The more common blood-borne metastases were not found.

It is not surprising that the tumor did not show any clinical regression or subsequent pathologic changes attributable to the radiation therapy. Unfortunately, the patient's poor condition made radiation

therapy impossible after a tumor dose of 2,200 r was given. It might be argued that the patient did not live long enough for any radiation induced tumor changes to become manifest. The general impression gained from reading the scant literature on this subject is that these tumors are almost always radio-incurable. However, they are frequently radio-responsive to a moderate dose of therapy.

CASE II. A fifty-five year old white male entered Henry Ford Hospital on August 22, 1960 with a two and one-half month history of painful, difficult swallowing. He denied nausea, vomiting, hematemesis, significant voice change, or melena. He had a twenty pound weight loss in three months.

Physical and laboratory findings were noncontributory. Examination of the ears, nose, and throat, including direct laryngoscopy, was negative as was thyroid scanning. Roentgenograms of the esophagus (Fig. 4) were obtained and because of the findings, esophagoscopy and biopsy were performed. The esophagoscopist described mild indentation of the posterior cervical esophagus but the biopsy did not reveal any abnormality.

Surgery subsequently showed the defect to be a hard, 4 by 4 cm. encapsulated mass lying within the musculature of the posterior esophagus just below the level of the cricopharyngeal muscle. The tumor was completely removed.

Pathologic examination of the surgical specimen revealed a bizarre, compact pattern of giant cells with peripheral nuclei, elongated strap cells, small round cells, and "racquet" cells intermixed with striated muscle fibers. There was a scanty amount of eosinophilic cytoplasm. PAS with and without diastase digestion showed the presence of a large amount of glycogen in the tumor. These latter findings and the absence of wiry reticulum between the tumor cells indicated the tumor to be of striated muscle origin. The final diagnosis was rhabdomyosarcoma.

Comment. The embryogenesis of the tumor in this case is very likely the same as in Case I. The growth characteristic is probably one of slow growth with sudden acceleration. Again, the growth stimulus remains unknown. Because of complete surgical enucleation of the tumor, radiation therapy was not indicated at this time. The patient has remained symptom free.

SUMMARY

Two cases of primary upper gastrointestinal tract rhabdomyosarcomas have been presented. Our experince in regard to the roentgen findings, treatment and pathology of this very rare tumor is discussed.

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The authors wish to thank Dr. Roy Patton for the interpretation of the pathologic material. The helpful suggestions of Drs. William R. Eyler and Robert J. Bloor are also gratefully acknowledged.

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GASTRODUODENAL INTUSSUSCEPTION

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INTUSSUSCEPTION in the intestinal tract occurs rather frequently, and gastroduodenal intussusception is not rare, although the diagnosis is seldom made preoperatively. The first report of roentgenologically demonstrated gastroduodenal invagination was that of Lönnerblad[1] in 1933, who presented 2 cases.

In that report he described in detail the roentgenologic criteria for the diagnosis of intussusception, *i.e.*, the characteristic contour of the mucosa and the distinctive appearance of the apex of the intussusceptum when contrast material is employed. The same criteria are valid for the relatively common ileocolic intussusceptions seen in children. In children these invaginations are rarely caused by pathologic alterations, while in adults they are almost always the result of pathologic processes, such as polyps, tumors, foreign bodies, etc.

In 1939 Zdansky[4] reported 1 case, and in 1955 Mauthe and Zwicky[3] reported 2 cases of gastroduodenal invagination which had been diagnosed roentgenologically. Marshak *et al.*[2] described in 1951 a case which was intrepreted roentgenologically as a tumor in the descending part of the duodenum, but which proved on operation to be an intussusception of a tumor from the greater curvature in the pyloric antrum. In their paper, the authors gave a summary of a number of cases of gastrointestinal invagination, but they found only 2 cases in which the diagnosis had been made preoperatively, and these were the 2 cases of Lönnerblad.[1]

It is probable that the diagnosis is rarely made by the roentgenologist because, in most instances, the invagination is a labile condition in which the intussusceptum moves in and out. There appears to be a certain periodicity in the symptomatology which supports this assumption. The typical findings are most readily obtained when the intussusceptum is incarcerated, with the pylorus as the hernial orifice, or when the patient is examined by chance just at the moment when the intussusception is present.

The present report is of a case in which the intussusceptum was incarcerated.

REPORT OF A CASE

A seventy-eight year old man, pensioned, was transferred to Sentralsykehuset for Östfold i Fredrikstad, Medical Department, from another hospital where he had spent a little less than three weeks. For the preceding two years he had suffered from a dyspepsia, but not to such an extent that he had sought medical advice until he suddenly had hematemesis about seven weeks before admission to Sentralsykehuset. He had subsequently twice had hematemesis which was relatively severe and was followed by melena. He grew debile, consulted a physician, and was admitted to the nearest hospital. Here the initial treatment was blood transfusions and his general condition gradually improved. Rectoscopy and roentgen examination of the colon and stomach revealed no definite pathologic signs except for sigmoid diverticula. However, as his condition later grew worse, he was transferred to the Medical Department at Sentralsykehuset.

On admission the patient was pale, slightly cyanotic, and complained of pains around the anal region and downward in the left thigh. Clinical findings included: pulse rate, 80 and regular; blood pressure, 135/75; hemoglobin, 7.59 gm. per 100 ml. of blood; heart, uncharacteristic systolic murmur; electrocardiogram, normal; abdomen, normal intestinal auscultation, soft, not sensitive, no intestinal tautness, and no palpable tumor.

Roentgenograms from the previous hospital admission were available and careful scrutiny revealed in one of them an alteration in the descending part of the duodenum, which indicated the need for further examination. On the new roentgenograms the typical contours seen in intussusception were found as well as a pronounced apex of the intussusceptum (Fig.

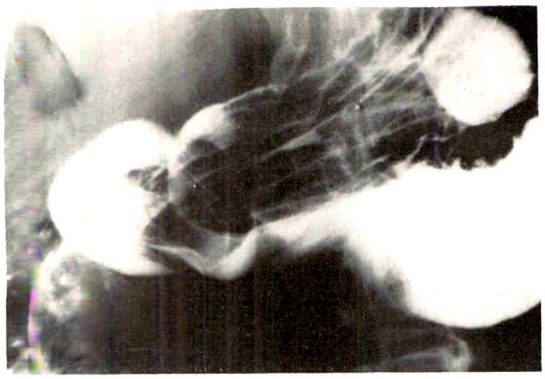


Fig. 1. Pronounced longitudinal stripes—the stalk—surrounded by rings of contrast material in two layers.

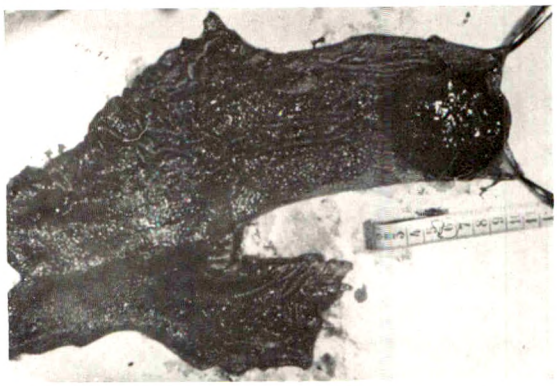


Fig. 3. The gastric specimen spread open with the tumor attached to the upper part of the anterior wall of the fundus.

1 and 2). On the basis of these findings the Roentgen Department made the diagnosis: gastroduodenal intussusception. The patient was transferred to the Surgical Department and was operated at once.

The roentgenologic diagnosis was confirmed. We cite from the surgeon's (Rosseland) description: At first inspection, both the stomach and the duodenum appeared normal except that the pylorus seemed wide. Palpation relatively far down on the descending part of the duodenum revealed a fairly soft tumor, almost the size of a tennis ball. Extending from the tumor upward through the pylorus and to the posterior wall of the stomach a rope-like structure was palpable. There was a deep indentation in the fundus, the bottom of which could not be reached with a finger. It thus appeared that the tumor had its origin in the upper part of the fundus. Attempts to push the tumor into the stomach manually were of no avail, so gastrotomy was performed. A mucous stalk was revealed, and by pulling on this it was possible to draw the tumor up. There was a necrotic, bleeding area on the upper surface of the tumor, which had a broad base arising from the anterior wall of the stomach. The bleeding was rather profuse. As the tumor was located so high in the stomach, a subtotal gastrectomy was performed with the usual anastomosis. The portion of the stomach which was removed (Fig. 3 and 4) measured 30 cm. along the side of the greater curvature, and 15 cm. on the side of the lesser curvature. The specimen weighed 340 gm.

Histologic diagnosis: leiomyoma with necrosis.

The postoperative course was uncomplicated.



Fig. 2. Shortening and obliteration of the lesser curvature with indentation in the fundus (arrow, upper right) and an egg-shaped tumor in the descending part of the duodenum with pronounced apex invagination (arrows, left).



Fig. 4. The same specimen as in Figure 3 with the tumor intussuscepted.

Comment. It is not difficult to make the diagnosis when the characteristic contours are present (Fig. 1 and 2). The shortening of the stomach, the obliteration of the lesser curvature, the widening of the descending part of the duodenum and the marked apex of the intussusception are visible in Figure 2. There is also a central tunnel-shaped defect in the contrast material with axial stripes surrounded by rings (Fig. 1). These longitudinal stripes represent the innermost lumen of the tube—a stalk—while the circular rings of contrast indicate the middle and outer tubes formed partly by swelling of Kerkring's folds and partly by folding of the outer intestinal layer. This description is, on the whole, similar to that presented by Lönnerblad.[1]

SUMMARY

A case of gastroduodenal intussusception diagnosed preoperatively is reported. A short review of 5 cases found in the available literature is given.

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INTUSSUSCEPTION OF A MALIGNANT DUODENAL POLYP*

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THE incidence of polyps of the small bowel is relatively small, but of these about 45 per cent occur in the duodenum. Those reported have been benign. Infrequently, such polyps are complicated by intussusception. Recently, we examined a patient with a duodenojejunal intussusception secondary to a malignant polyp.

REPORT OF A CASE

A fifty-eight year old Caucasian male was admitted December, 1959, with a history of indigestion and occasional bloating of five to six years' duration. For the preceding two months, he had noted episodic distention associated with constipation and rectal bleeding. There was no weight loss. A large polypoid defect had been demonstrated in the duodenum on 2 different roentgen examinations. In view of the more recent symptoms, he was admitted for elective surgery.

His past medical history included a pituitary adenoma in 1955 treated with radiation therapy. Later he developed blindness of the left eye and adrenal steroid deficiency. He was well maintained on hydrocortisone.

Physical findings were within the limits of normal, except for the blindness. Routine laboratory studies were normal.

Roentgen Studies. The first examination was done at another hospital in 1954 at the onset of the patient's abdominal complaints. The study showed a large diverticulum arising from the descending loop of the duodenum, and an oval filling defect in the third portion of the duodenum, measuring 6 by 4 cm., without obstruction (Fig. 1). He was examined again in November, 1959, and the same abnormalities were demonstrated (Fig. 2). The filling defect appeared unchanged since the previous examination five and one-half years earlier. The roentgen interpretation was a benign tumor. Study at our hospital one month later again demonstrated the diverticulum and the tumor,



FIG. 1. *May, 1954:* initial study. Note the large diverticulum arising from the descending duodenum, and an oval filling defect in the third portion without intussusception.

with the additional complication of extensive intussusception (Fig. 3, *A* and *B*).

The preoperative diagnosis was duodenal adenoma. At surgery, a polypoid tumor approximately 5 cm. in diameter was found in the second portion of the duodenum. Since the muscular coat seemed to be invaded, a frozen section was obtained. Well-differentiated adenocarcinoma was reported. Therefore, a subtotal gastrectomy, partial duodenectomy and antecolic gastrojejunostomy were performed. No other tumor was seen. Since surgery, the patient has done well. When last seen five months after the operation, he was asymptomatic and was working full time.

Histologically, the tumor proved to be a pedunculated adenomatous polyp with a focal area of well-differentiated adenocarcinoma showing limited invasion of the stroma (Fig. 4).

DISCUSSION

Polyps of the small bowel are most fre-

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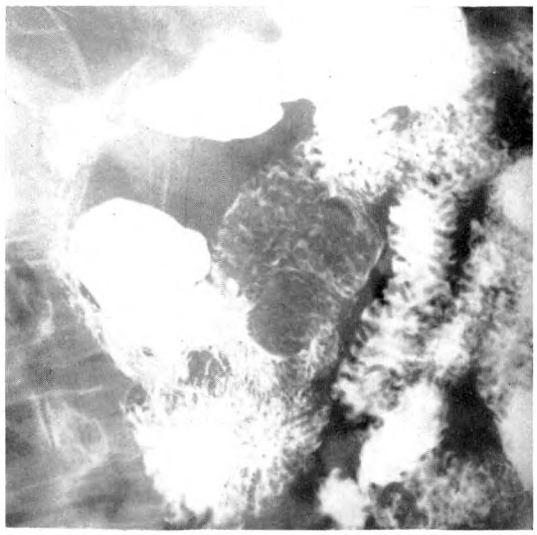


FIG. 2. *November, 1959:* repeat study five and one-half years after Figure 1. The same abnormalities are demonstrated. The filling defect appears unchanged. Once again there is no evidence of intussusception.

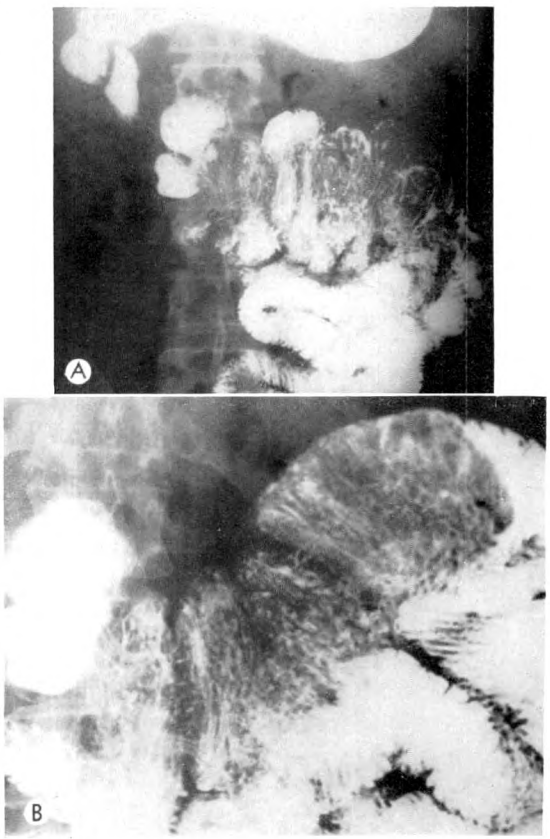


FIG. 3. *December, 1959:* one month after Figure 2. (*A*) The diverticulum and the tumor are again demonstrated, with the additional complication of extensive intussusception. (*B*) Another view of the intussusception enlarged for detail.

quently asymptomatic, and discovered at autopsy. While vague gastrointestinal symptoms occur occasionally, polyps which become symptomatic generally present with obstruction, especially intussusception, or bleeding. River *et al.*,[6] in their comprehensive review of benign small bowel neoplasms, found them to be the most common cause of intussusception in adults. However, this complication is usually of ileal origin. Prolapse of gastric mucosa or polyps with gastroduodenal intussusception are also seen with some regularity, but intussusception of a duodenal polyp is rare. River *et al.* found 13 references to such in the world literature, and since their review, we have learned of 4 others,[2–4] all benign. At least 1 of these, in addition to our case, intussuscepted beyond the ligament of Treitz.

The rarity of duodenal intussusception seems best explained on an anatomic basis. The duodenum differs from the rest of the small bowel in that it has no mesentery. The first portion is somewhat mobile, but the remaining three portions are fixed by the overlying peritoneum to the posterior abdominal wall, liver and pancreas. In addition, the duodenojejunal flexure is held firmly in place by a fibrous and muscular band, the ligament of Treitz.

Roentgen examination is the most valuable method in the diagnosis of benign duodenal tumors, and their differentiation from biliary, pancreatic or peptic ulcer disease. Typically, benign tumors present as well-defined regular filling defects—usually circular, sometimes multilocular. A pedicle is considered by many to favor benignancy. Ulceration may be present, but the mucosal pattern is maintained.

Histologically, the majority of duodenal polyps are papillary adenomas. Of the polyps which intussuscepted, only four exceptions were found—1 fibroadenoma,[6] 2 fibromyomas[6] and 1 myoma.[4]

Malignant lesions of the duodenum are

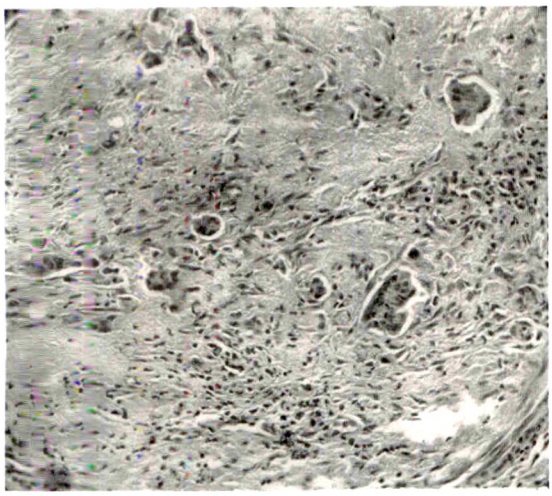


FIG. 4. Section of malignant portion of the polyp showing the presence of malignant cells in vascular channels (×200).

infrequent with an estimated incidence of 0.235 per cent based on a total of 487,695 autopsies.[3] Of these, 60 per cent occur in the periampullary region. The clinical picture correlates with the morphologic characteristics of the lesions. These may be categorized as follows: (1) obstructing lesions, (2) ulcerating lesions, (3) lesions penetrating into the pancreas and (4) lesions encroaching upon the ampulla of Vater. Accordingly, the major symptoms will be (a) vomiting, (b) bleeding, (c) gnawing pain unrelieved by food or alkali and (d) obstructive jaundice. Weight loss often provides the strongest clinical suggestion that the underlying lesion is malignant.

Roentgen examination again is the most valuable procedure in the diagnosis of malignant duodenal tumors. Brenner and Brown[1] outlined the important abnormalities seen in malignant lesions of the duodenum as follows: (1) annular, infiltrating or ulcerative defects, (2) effacement and thickening of the mucosa, (3) irregular polypoid defects which narrow the lumen, (4) dilatation of the duodenum above a constricted area and dilatation of the stomach with gastric retention, and (5) rigidity of the duodenal wall.

The majority of malignant duodenal lesions are adenocarcinomas. The next most common are lymphosarcomas with a ratio for the two of approximately ten to one. Leiomyosarcomas, carcinoids and other tumors are observed very rarely. An estimated 45 per cent of small bowel carcinomas occur in the duodenum, in contradistinction to sarcomas and carcinoids which occur more frequently in other parts of the small bowel. Where histologic detail has been reported, duodenal carcinomas have been papillomatous in configuration. No report of a carcinoma associated with a duodenal polyp was found. The question of malignant degeneration in polyps comes forcibly to mind, but is beyond the scope of this case report.

SUMMARY

1. A case of a fifty-eight year old Caucasian male having a duodenal polyp which intussuscepted and which proved to contain focal adenocarcinoma is presented.

2. Duodenal intussusception is briefly discussed.

3. Benign and malignant lesions of the duodenum are compared in regard to incidence, clinical behavior, roentgen appearance and histology.

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A ROENTGENOLOGIC REMISSION IN ULCERATIVE COLITIS

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ULCERATIVE colitis is generally considered to be a chronic disease characterized by remissions and exacerbations and pursuing a mild course in most, and a rapidly progressive, occasionally fatal, course in others. Complete clinical remissions are not unusual, but it is generally not appreciated that chronic ulcerative colitis may have a complete roentgenologic remission. Generally, the changes of far advanced ulcerative colitis have been regarded as permanent. Indeed, when shortening of the colon, narrowing of the lumen, and stricture formation have occurred, it is difficult to understand how the process could be reversible. The following report illustrates a far advanced case of ulcerative colitis that had a complete clinical and an apparent roentgenologic remission.

REPORT OF A CASE

The patient was a nine year old white female referred to Jefferson Medical College Hospital on January 30, 1948, with a diagnosis of ulcerative colitis.

Early in 1946, she developed what her parents described as "intestinal grippe," which consisted of fourteen to twenty watery stools per day containing mucus and blood. The episode lasted one week and subsided spontaneously. There were two more occurrences of diarrhea, which subsided without treatment, during the remainder of 1946. In August, 1947, frequent loose bowel movements recurred and gradually increased in severity. Because of the persistence of diarrhea, she was admitted to another hospital in December, 1947, and a diagnosis of ulcerative colitis was made. When she failed to respond to therapy, she was referred to Jefferson Medical College Hospital.

Family history revealed that she was the oldest of four sisters. She was described as above average in intelligence by her mother, was apparently well adjusted, and came from a reasonably happy home.

Physical examination disclosed a thin well-developed white female child who was 54 inches tall and weighed 54 pounds. The temperature was 99.2° F. orally. The remainder of the physical examination was not remarkable. Proctosigmoidoscopy revealed a granular, engorged and extremely friable rectal mucosa, and bleeding occurred with slight trauma. The findings were felt to be characteristic of chronic ulcerative colitis. The laboratory studies were within normal limits. Barium enema examination (Fig. 1*A*) was performed and was interpreted as being consistent with ulcerative colitis. After a slight clinical improvement, the patient was discharged on February 6, 1948.

In April, 1950, the patient was readmitted because of frequent bloody bowel movements. Since her previous discharge in February, 1948, she had had four to six loose stools per day. About six weeks before admission, she had begun to have six to fifteen watery, frequently bloody, stools per day. The physical examination was not remarkable. Proctosigmoidoscopy revealed the perineal skin to be reddened and tender, and the mucosa was thickened, friable, and showed ulceration. Barium enema examination (Fig. 1*B*) showed progression of the ulcerative colitis. The patient was given a course of ACTH, followed by cortisone, and marked improvement was noted with the stools becoming formed and less frequent. After June, 1950, there was steady clinical improvement. Two brief exacerbations of diarrhea in July, 1951, and November, 1952, subsided spontaneously. Frequent proctoscopic examinations revealed a gradual but steady decline in the mucosal inflammation. In November, 1952, the colon showed little change roentgenologically (Fig. 1*C*), but one year later (Fig. 1*D*)

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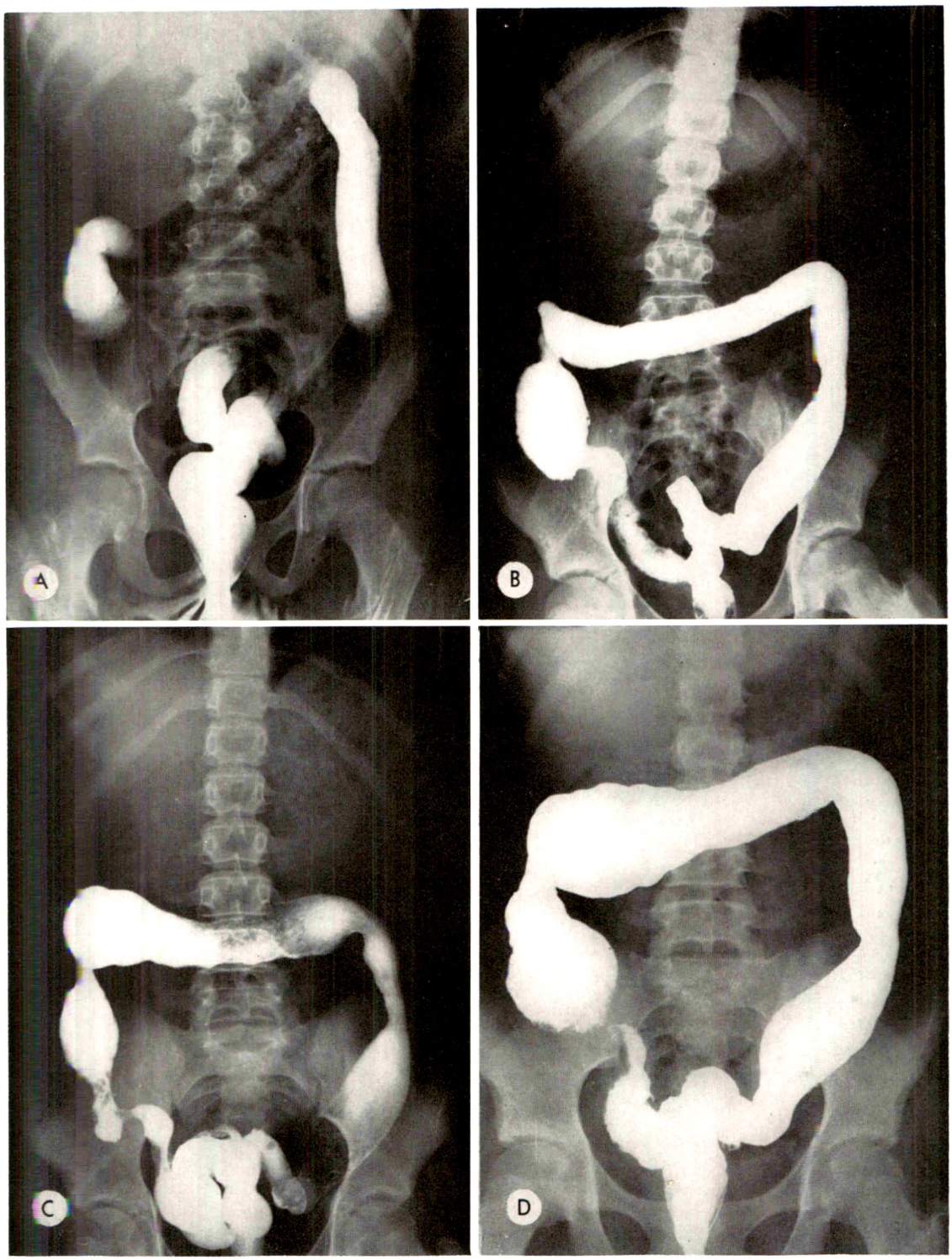


FIG. 1. (*A*) *January, 1948:* The colon is narrowed and somewhat shortened, and there is complete loss of haustral markings. The edge of the barium column is irregular. (*B*) *April, 1950:* Further shortening has occurred and a stricture is evident at the hepatic flexure. The ileocecal valve is patent, and the terminal ileum also appears to be involved. (*C*) *November, 1952:* Shortening of the colon is still evident but there is more distensibility. Stricture of the hepatic flexure is still present. (*D*) *October, 1953:* The colon has lengthened somewhat, and is more distensible. The stricture at the hepatic flexure is still present.

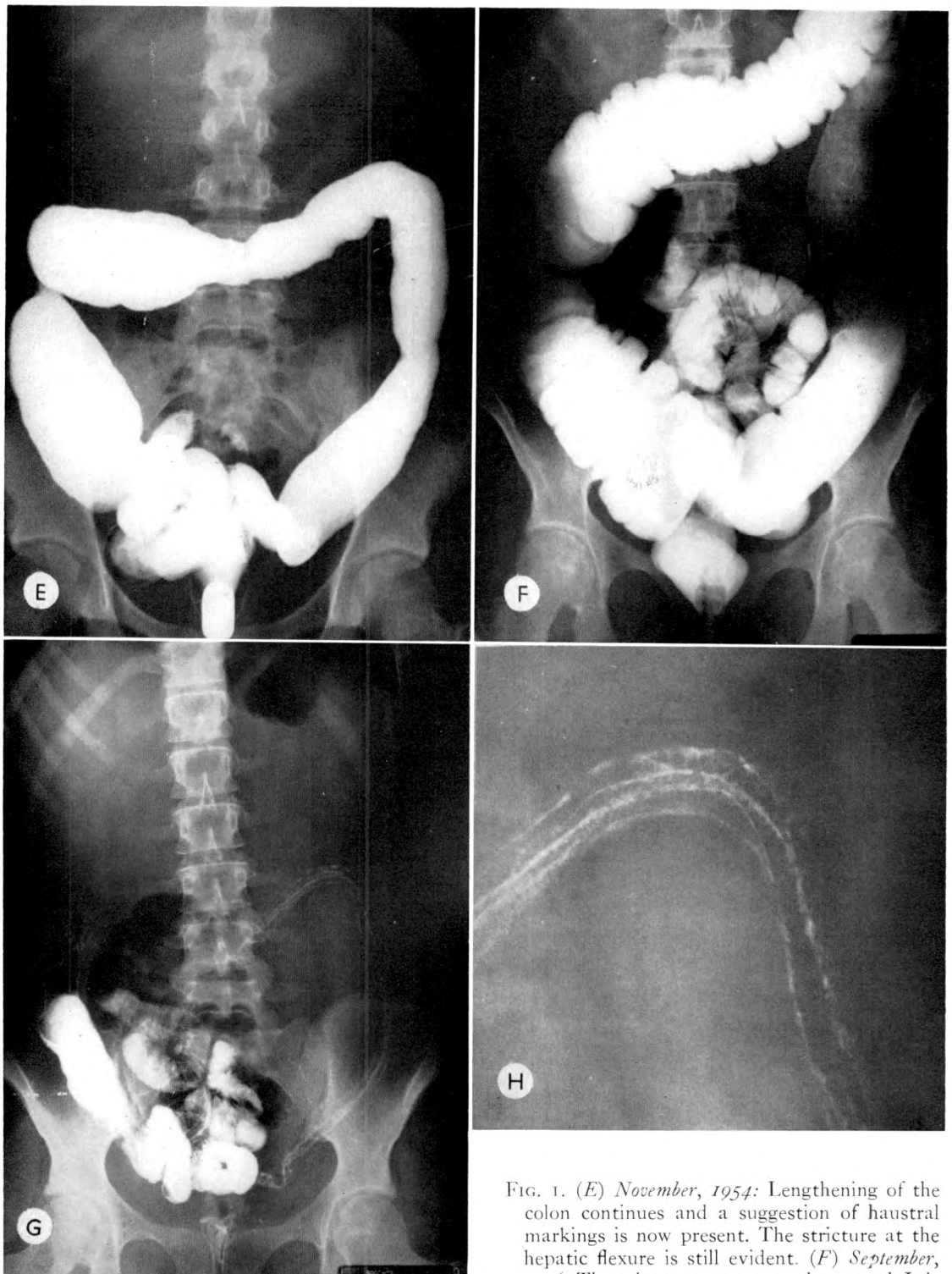


FIG. 1. (*E*) *November, 1954:* Lengthening of the colon continues and a suggestion of haustral markings is now present. The stricture at the hepatic flexure is still evident. (*F*) *September, 1956:* The colon now appears to be normal. It is distensible, haustral markings are present, and it is now of normal length. The hepatic flexure is not well demonstrated. (*G* and *H*) Postevacuation roentgenogram and close-up study of the mucosal pattern at the splenic flexure show a cobble-stone appearance of the mucosa with longitudinal furrowing. The mucosa is abnormal.

the bowel exhibited definite improvement, which continued in 1954 (Fig. 1*E*). She was completely asymptomatic in September, 1956, and no evidence of activity was noted at proctoscopy. The roentgenologic appearance of the colon (Fig. 1*F*) was normal, but in the postevacuation roentgenograms (Fig. 1, *G* and *H*) the mucosal pattern was still definitely abnormal. Since September, 1956, her family physician has reported that she has married, has had an uneventful pregnancy, and has had no exacerbations of ulcerative colitis.

DISCUSSION

The characteristic roentgenologic changes of ulcerative colitis are well known. In the early stages, the alterations are limited to the mucosa. The edges of the barium column appear serrated, and there is hypertonicity. Mucosal ulcerations can be demonstrated in many cases. Later, loss of haustral markings occurs, and eventually the colon shortens and becomes narrow. Stricture formation is not uncommon. Ultimately, the picture is one of a markedly shortened, narrowed, pipestem colon with an irregular mucosal pattern that shows ulceration and pseudopolypoid changes.

In our case, the early roentgen studies (Fig. 1, *A*, *B* and *C*) showed the typical roentgenologic appearance of a well-established ulcerative colitis. The large bowel is markedly shortened and narrowed and there is stricture formation near the hepatic flexure. In addition, the colon is not distensible, and the mucosa shows the typical changes of the disease. In later roentgenograms (Fig. 1, *D* and *E*) there is gradual improvement in the appearance of the large bowel, and the narrowing and shortening are less marked. In the last series of roentgenograms the barium filled colon appears normal (Fig. 1*F*), but in the postevacuation study (Fig. 1, *G* and *H*) there is distortion and beading of the mucosal pattern with longitudinal furrowing, showing it to be still definitely abnormal. Thus, in our case, when the barium filled colon alone is used as a criterion, there appears to be complete roentgenologic remission of ulcerative colitis. But, if the appearance of the mucosal pattern as seen on the postevacuation roentgenogram is employed to judge remission, the unmistakable traces of the disease remain.

Shanks and Kerley[9] state that in ulcerative colitis, "*restitutio ad integrum*" takes place only if cure is obtained early in the disease, and Feldman[3] describes the changes as "permanent." Others[2,4,6,8] use terms such as "stenosed," "cicatricial," "fibrosis," and "scarring" to imply that the far advanced changes in ulcerative colitis are not reversible. However, it was pointed out by Bockus *et al.*[1] that occasionally a colon which is markedly stenosed due to advanced ulcerative colitis can be distended by barium enema during a clinical remission, and he illustrated his point by citing a case that showed apparent roentgenographic improvement during a remission.

During the past twenty years, occasional cases have been reported that showed improvement in the roentgenologic appearance of the colon, and, in some cases, the diseased colon apparently has become normal. Ricketts, Kirsner, and Palmer[7] reported complete roentgenologic recovery in 5 cases of ulcerative colitis, but the appearance of the mucosal pattern is not mentioned. Kirsner, Palmer, and Klotz[5] cited 4 cases of complete roentgenologic remission. In 1 case, the mucosal pattern is mentioned as abnormal during an exacerbation, but the reversibility of the mucosal abnormality later is only implied, and not definitely stated.

In reviewing the literature in all cases so far reported, the reversion to normal has been demonstrated only by the barium filled colon, and the mucosal pattern as seen in the postevacuation roentgenogram has not been shown. Since the mucosa is the primary site of involvement in ulcerative colitis, it would seem logical that the mucosal pattern should be demonstrated to be normal when attempting to establish a complete roentgenologic remission in ulcerative colitis.

SUMMARY AND CONCLUSION

A patient with far advanced ulcerative colitis that showed striking improvement both clinically and roentgenologically is reported. Attention is drawn to the fact that the roentgen appearance of the barium filled colon alone is a poor criterion for judging complete reversal of the process. A normal mucosal pattern should be demonstrated before complete roentgenologic remission can be claimed.

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PNEUMATOSIS OF THE INTESTINES

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PNEUMATOSIS or gas cysts of the intestine (pneumatosis intestinalis cystoides) is a descriptive name denoting an abnormal collection of gas in the walls of the gastrointestinal tract. Numerous case reports and reviews of this condition have appeared in the literature since its first description by Du Vernoi in 1738.

Pneumatosis of the intestine is not a disease entity. It is a symptom complex accompanying abdominal diseases of different etiology and occurring in every age group of patients (from three days to seventy years of age).

Our purpose is to report upon that group of pneumatosis seen in adult patients who show marked weight loss, malnutrition, or even emaciation, and to present the results of treatment. As pneumatosis is of rather rare occurrence, there are uncertainties about its etiology, course and treatment. The observations made on our patients may throw some light on its etiology and may indicate the treatment of choice.

REPORT OF CASES

CASE 1. J.J., a thirty-three year old male, was admitted as an emergency patient with the provisional diagnosis of perforated peptic ulcer. The diagnosis was based upon a past history of duodenal ulcer and the presence of a marked hydropneumoperitoneum on fluoroscopy.

For seven days prior to admission he had vomited after every meal and had noted painless increasing abdominal distention and splashing sounds emanating from his abdomen. During the last six months the patient had lost 6 kg. in weight.

Physical examination showed a markedly undernourished, dehydrated, but comfortable, patient. His height was 175 cm. and weight 55.5 kg. The abdomen was extremely distended, but soft. Shifting dullness was present. The rest of the physical examination was negative. Urinalysis and blood cell count were within normal limits.

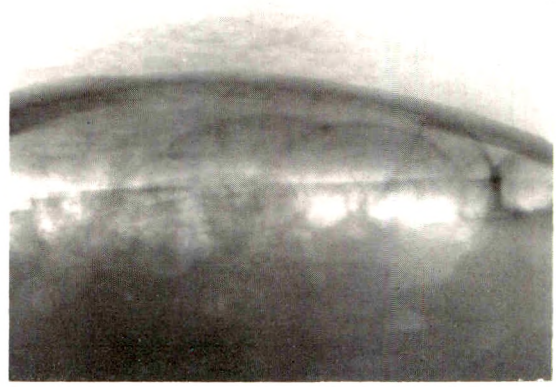


FIG. 1. Case 1. Scout roentgenogram of the abdomen using horizontal rays in the supine position shows the extensive hydropneumoperitoneum.

Scout roentgenograms of the abdomen with horizontal rays (Fig. 1 and 3A) revealed extensive hydropneumoperitoneum, multiple cysts under the right diaphragm, interposition of intestinal loops between liver and diaphragm and absence of the liver shadow. On the scout roentgenogram using vertical rays in the supine position (Fig. 2), the liver shadow appeared in its normal position and the cysts were visible over the entire abdomen.

Because of the absence of clinical signs of an acute abdomen, a diagnosis of pyloric stenosis associated with pneumatosis intestinalis cystoides was made. Rehydration, gastric suction and parenteral alimentation were commenced.

In order to relieve the abdominal distention, 1,500 cc. of fluid was removed by abdominal tapping on the day of admission. This fluid, which was yellow colored, was sterile on bacteriologic examination. Guinea pig inoculation was negative for tubercle bacilli. After adequate rehydration the patient was fed on a concentrated high caloric soft diet.

Serum electrolytes and liver function tests were normal. Barium studies of the gastrointestinal tract showed a marked pyloric stenosis. The colon was normal; however, the

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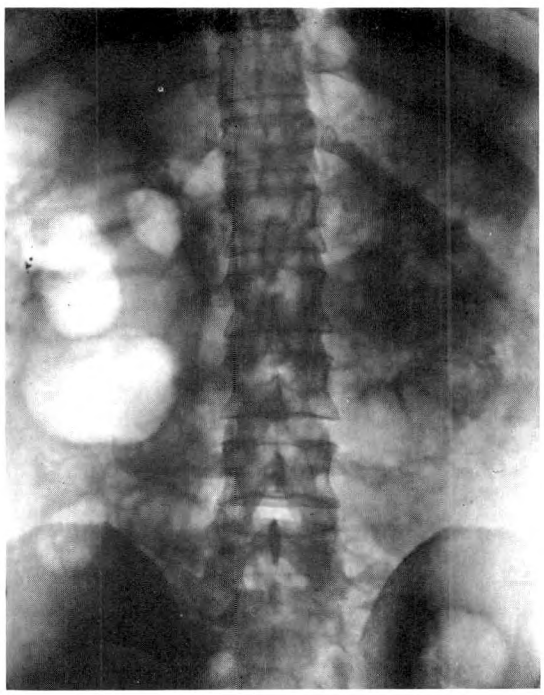


FIG. 2. Case 1. Scout roentgenogram using vertical rays in the supine position shows multiple cysts scattered throughout the abdomen.

small intestine was noted to be interposed between the liver and diaphragm. Repeated scout roentgenograms showed a gradually diminishing pneumoperitoneum, disappearance of free fluid in the peritoneal cavity and some reduction in the number of cysts (Fig. 3, *A*, *B* and *C*).

The patient was prepared for surgery by repeated blood transfusions, amigen, glucose and electrolyte infusions. Operation was carried out on the twenty-third day of hospitalization. The day before operation a small pneumoperitoneum and numerous cysts were still visualized on roentgenograms.

Before opening the peritoneal cavity, peritoneal air was obtained for gas analysis through a cannula by means of a vacuum apparatus. The stomach was found to be dilated and have thickened walls, and an almost complete pyloric obstruction due to a chronic duodenal ulcer was seen. Five thousand cubic centimeters of yellowish ascitic fluid were removed from the peritoneal cavity.

A segment of the distal ileum, about 80 cm. long, was covered by numerous gas cysts, 1–3 cm. in diameter, arranged in clusters on the mesenteric and the antimesenteric borders of the bowel. They were round, of elastic consistency, and translucent. Some of them adhered to each other and to the intestinal wall. Others were single, attached to the free end of a thin avascular pedicle, often bluish in color, and contained small amounts of fluid (Fig. 4). Segments of normal bowel were observed between the masses of gas cysts, as well as fine white scars and coarse adhesions between the loops. The mesentery was edematous, and signs of mild inflammatory reaction along the affected segments were noted. The mesenteric lymph nodes were enlarged. The gas in the cysts could not be pressed from one cyst into another or into the intestinal lumen. On pressure the cysts burst. There was no other intra-

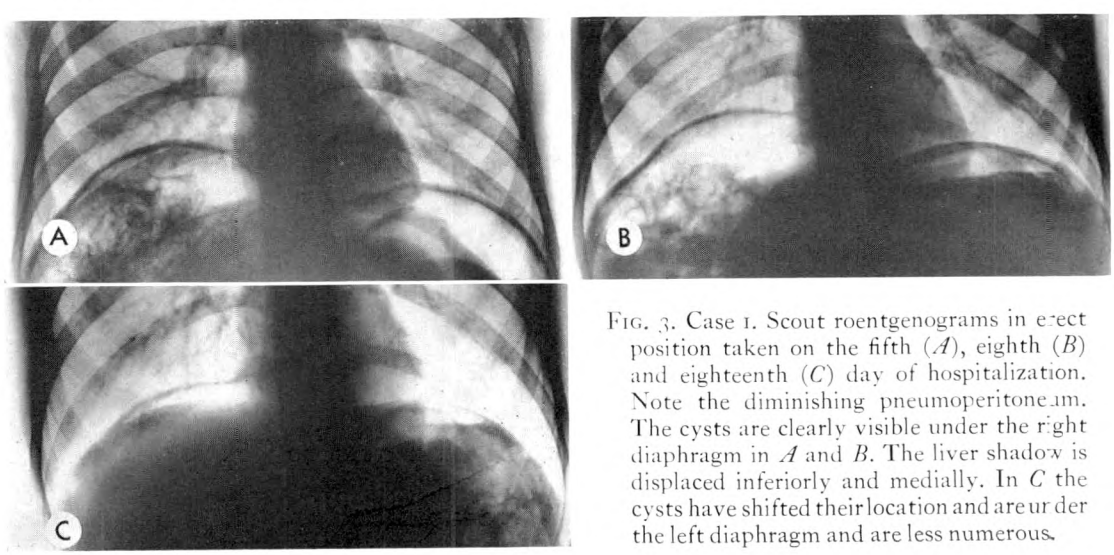


FIG. 3. Case 1. Scout roentgenograms in erect position taken on the fifth (*A*), eighth (*B*) and eighteenth (*C*) day of hospitalization. Note the diminishing pneumoperitoneum. The cysts are clearly visible under the right diaphragm in *A* and *B*. The liver shadow is displaced inferiorly and medially. In *C* the cysts have shifted their location and are under the left diaphragm and are less numerous.

abdominal pathology. One large gas cyst was excised intact so that a gas analysis could be obtained. A transmesocolic gastrojejunostomy and a bilateral vagectomy were performed. The analysis of the gas obtained from the peritoneal cavity and from the resected cyst showed 79 volume per cent nitrogen, 19 volume per cent oxygen and about 1 volume per cent CO_2.

The postoperative course was uneventful. A scout roentgenogram of the abdomen taken on the eighth postoperative day showed complete disappearance of the cysts (Fig. 5).

On the twelfth postoperative day the patient was discharged. He gained 10 kg. in weight during the first seven postoperative weeks and 22 kg. in the six months following his operation. Roentgenologic re-examination six, twelve, eighteen, twenty-four and forty months after surgery did not disclose any cysts or pneumoperitoneum.

The patient is at present in excellent health.

Comment. This patient was in an extremely poor nutritional state due to severe pyloric obstruction. He presented the typical roentgen findings of pneumatosis intestinalis cystoides with marked ascites of the reactive exudative type. The pronounced hydropneumoperitoneum was in sharp contrast to the mild clinical picture. No urgent surgery was done. On conservative treatment the pneumoperitoneum receded gradually and the cysts became less numerous. Eight days after the gastrojejunostomy and vagectomy, all the cysts and the pneumoperitoneum disappeared and did not recur during a three year follow-up. To our knowledge this is the shortest reported interval for the postoperative disappearance of gas cysts.



Fig. 4. Case 1. Appearance of a cyst-bearing loop at operation. Note the long pedicles of the cysts.

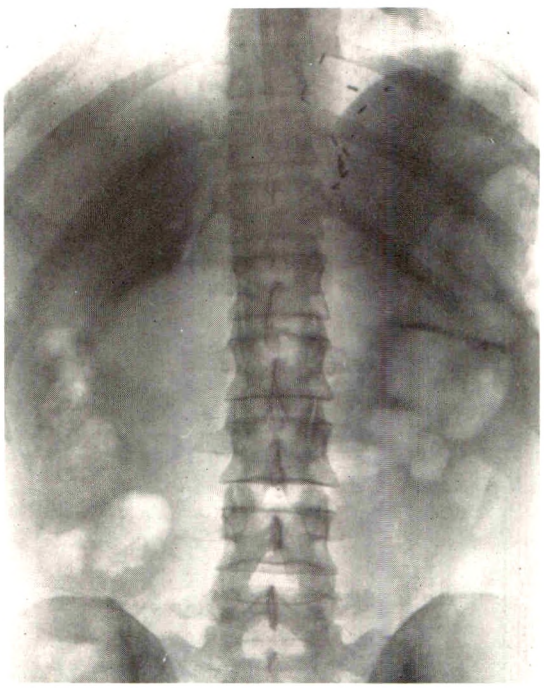


Fig. 5. Case 1. Scout roentgenogram on the eighth postoperative day. No cysts are visible.

Case II. J.M., a seventy year old male, was admitted as an emergency patient because of abdominal pain, intractable vomiting, a distended abdomen and severe dehydration. The past history revealed a roentgenologically proved duodenal ulcer of twenty years' duration.

On physical examination the patient was extremely dehydrated and emaciated. His weight was 46 kg. and height 174 cm. Definite signs of avitaminosis were present in the angles of the mouth, buccal mucosa and on the skin of the forearms and the hands. Pitting edema of the lower extremities was present.

Scout roentgenograms of the abdomen (Fig. 6) showed pneumoperitoneum and the other characteristic findings of pneumatosis intestinalis cystoides. A diagnosis of pyloric obstruction, pneumatosis intestinalis cystoides and severe malnutrition was made. Rehydration, gastric suction and parenteral alimentation were started.

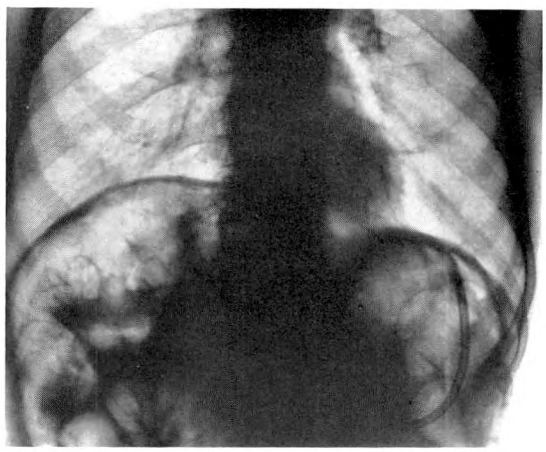


Fig. 6. Case II. Roentgenogram in the erect position shows an appearance similar to that seen in Case 1 (Fig 3*A*).

Laboratory examinations including urinalysis, blood cell count, liver function tests and serum electrolytes were within normal limits.

Roentgen examination on the fourth day of admission showed severe pyloric obstruction and rounded small filling defects in the lumen of the small intestine. Loops of small intestine were interposed between the liver and the diaphragm. These loops did not change their location with change of the patient's position. The transit of barium in the small intestine was markedly slow. A barium enema study was normal. Laminagraphy of the right upper abdomen (Fig. 7) showed adhesions between the walls of the intestine and the diaphragm.



Fig. 7. Case II. Laminagram of right upper abdomen. Note the large cyst below the diaphragm laterally and the adherence of cysts and intestine to diaphragm.

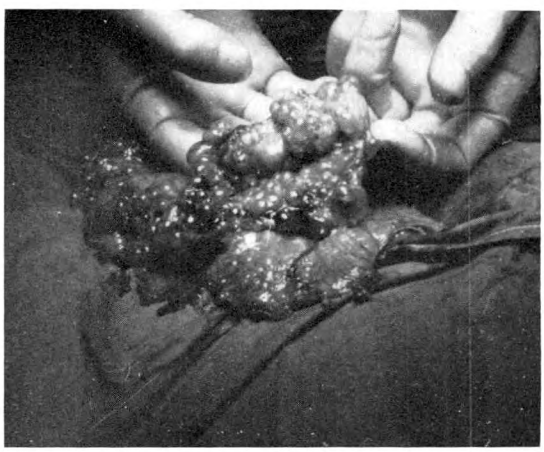


Fig. 8. Case II. Appearance of the cyst-bearing, doubly-rotated loop at laparotomy.

Preparations for surgery included blood transfusions, amigen and electrolyte infusions and high doses of vitamins. The patient was operated on seven days after admission. Laparotomy revealed a distended, thick-walled stomach and almost complete pyloric obstruction due to a duodenal ulcer. The distal part of the jejunum, with numerous large gas cysts attached, was interposed between the liver and the right diaphragm. There were numerous adhesions between the loops and the right diaphragm. This segment was doubly rotated on the axis of its mesentery (Fig. 8), the bowel wall was congested, the mesenteric vessels engorged, but no thrombotic process was evident. The segment of bowel proved to be viable after relieving the torsion. Another segment of small bowel, 130 cm. in length and extending to within 20 cm. of the ileocecal valve, was covered by multiple subserosal cysts varying in size from 1 to 5 cm. in diameter. They were thin-walled, translucent and round, and appeared on the mesenteric and antimesenteric borders of the bowel. They were either packed closely together and attached to each other and to the intestinal wall by a broad base, or they were single on the free end of an avascular pedicle. Short segments of normal small bowel were scattered between the masses of gas cysts. Signs of subacute and

chronic inflammation, with fine multiple adhesions and delicate white scar formations, were present between the wall of the intestines and the mesentery.

A transmesocolic gastrojejunostomy was performed and a large cyst was excised for gas analysis. The adhesions between the small intestinal loops and right diaphragm were divided.

The postoperative course was uneventful. The signs of avitaminosis disappeared gradually. The patient gained 6 kg. in five weeks, and most of the gas cysts disappeared in that period as indicated by repeated flat roentgenograms of the abdomen. Six months postoperatively no cysts were visible roentgenographically. The result of the gas analysis of the cyst was the same as in Case 1.

The patient was discharged thirty-eight days postoperatively and followed-up for two years. Repeat roentgenologic examinations revealed no evidence of the cysts.

Comment. This patient was emaciated due to long standing pyloric obstruction. The preoperative diagnosis was pyloric stenosis associated with pneumatosis intestinalis cystoides. No urgent surgery was undertaken. Elective gastrojejunostomy was performed after adequate preparation. The patient made an excellent recovery and the cysts gradually disappeared, the last of them six months after operation. Today, two years postoperatively, his general condition is satisfactory.

Case III. F.S., a fifty-four year old male, was admitted as an emergency patient because of severe vomiting and vague abdominal pains. He had been vomiting after meals during the three months prior to admission. The past history revealed a duodenal ulcer (proved by roentgen examination) of sixteen years' duration, two episodes of hematemeses (six years and four years prior to admission), 8 kg. loss of weight and fainting spells during the last three months.

On admission the patient appeared markedly undernourished and dehydrated. His skin was atrophic and scaly. The abdomen was somewhat distended but no signs of peritoneal irritation were detectable.

Scout roentgenograms of the abdomen in erect position showed a moderate pneumoperitoneum. An unusual finding was a 2–5 mm. wide strip of air shadow outlining the stomach. This air strip was present on both the lesser and greater curvature as well as in the anterior wall of the stomach. Additional roentgenograms showed the air strip unchanged in its relation to the cavity of the stomach and its wall (Fig. 9, *A*, *B* and *C*), thus proving that it was trapped between the layers of the gastric wall. The stomach was markedly dilated and contained a large quantity of fluid.

The diagnosis of pyloric stenosis with gastric pneumatosis was made. No urgent surgery was deemed necessary. The patient was accordingly admitted for elective surgery after preparation by conservative treatment.

Urinalysis, blood cell count and liver function tests were all normal. The blood urea nitrogen was elevated due to extrarenal uremia explained by marked dehydration. There was severe electrolyte imbalance—hypopotassemia, hyponatremia, hypochloremia and metabolic alkalosis. This electrolyte imblance was completely corrected by the seventh day after admission by repeated blood transfusions and parenteral electrolytes. On the eighth day of hospitalization no free air was seen in the peritoneal cavity and only small bubbles of air could be detected in the stomach wall.

At laparotomy on the twelfth day after admission the stomach was found to be greatly dilated with thickened walls. Crepitation was felt on palpation of the stomach wall. Tight pyloric obstruction was present. No perforation was seen. No cysts were found on the small or large intestines, neither were cysts seen on the peritoneal surface of the stomach. Gastrojejunostomy with vagectomy and a feeding jejunostomy were performed.

The postoperative course was uneventful. The temporary feeding jejunostomy tube was withdrawn on the seventh postoperative day and the patient was discharged on the twelfth postoperative day, having gained about 4 kg. during his hospitalization of twenty-four days. At re-examination one year after surgery, the patient was in excellent condition. There was no air visible in the stomach wall.

Comment. This patient was admitted in a markedly undernourished condition due to prolonged vomiting caused by pyloric stenosis. The roentgen examination revealed the unique appearance of "gastric pneumatosis" in addition to a pneumo-

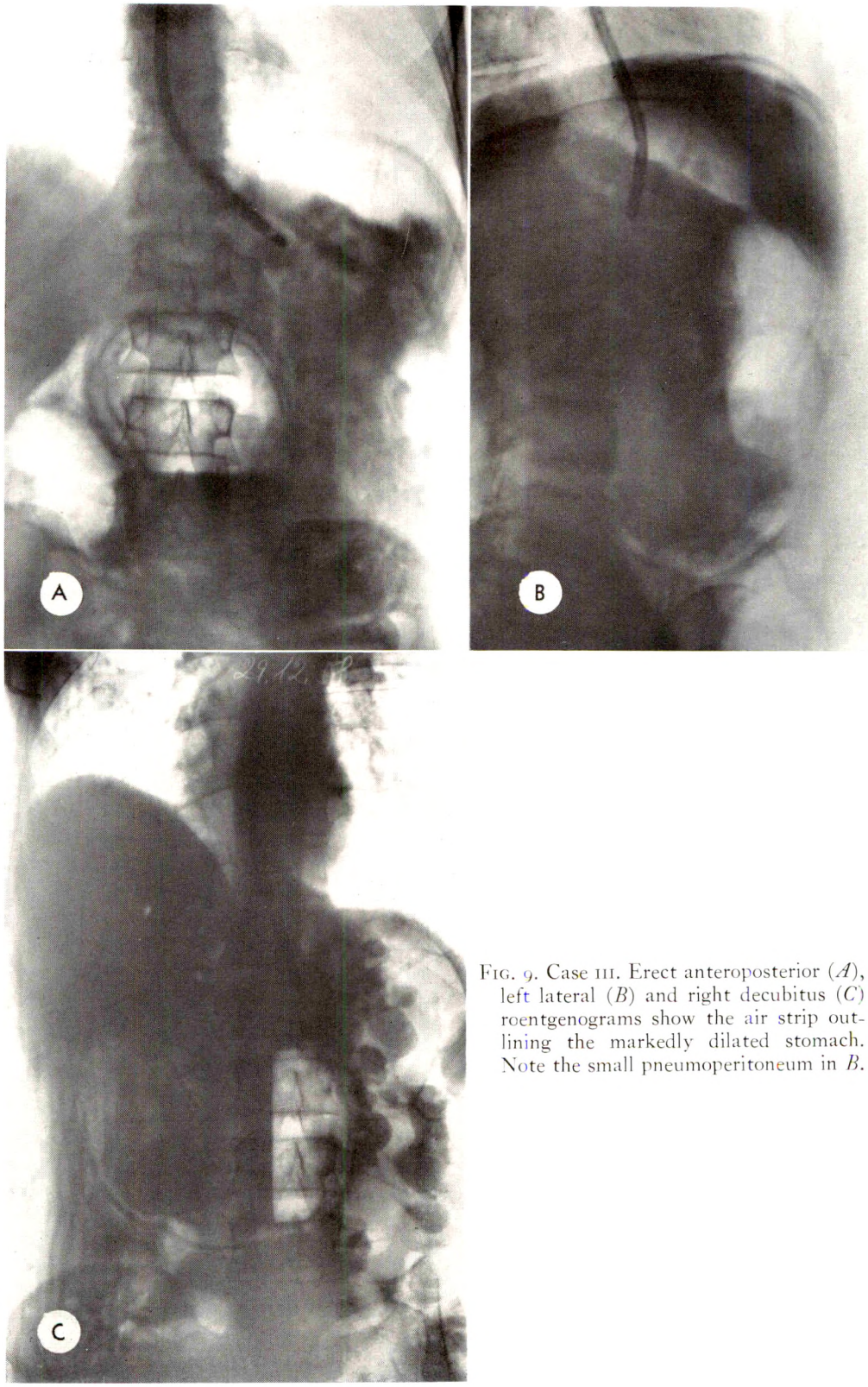


FIG. 9. Case III. Erect anteroposterior (*A*), left lateral (*B*) and right decubitus (*C*) roentgenograms show the air strip outlining the markedly dilated stomach. Note the small pneumoperitoneum in *B*.

peritoneum. No other signs of pneumatosis of the intestines were seen. After elective gastroenterostomy and vagectomy the patient recovered completely.

To our knowledge this is the first case in which this type of gastric pneumatosis has been roentgenologically demonstrated.

Case IV. U.A., a forty-four year old male, was admitted as an emergency patient because of severe vomiting and vague abdominal pains. His past history revealed that during the previous nine years he had had five episodes of sudden marked abdominal distention with vomiting and constipation. These episodes occurred at intervals of about one to two years and always after extreme physical and mental strain. On each occasion a pneumoperitoneum was diagnosed clinically and roentgenologically. Seven years previously, during his second episode, laparotomy was done (in Romania) but nothing abnormal was found. The pneumoperitoneum subsided on each occasion upon rest and nutritional improvement about six to seven weeks after its appearance.

The present episode of sudden abdominal distention occurred fourteen days after his arrival in this country from Romania. He had had quite a lot of trouble connected with his emigration, his arrival and with settling down anew.

On admission his abdomen was extremely distended, but no signs of an acute inflammatory or obstructive abdominal condition could be detected. His nutritional condition was rather poor. The rest of the physical examination was noncontributory.

Roentgen examination revealed a marked pneumoperitoneum with the presence of a delicate, curved linear shadow below the right diaphragm, resembling the wall of a gas cyst.

A diagnosis of recurrent pneumoperitoneum, probably due to pneumatosis intestinalis cystoides, was made. Urgent surgery was not indicated. The patient responded well to conservative treatment and was discharged for follow-up in the outpatient department. A barium meal study showed a normal esophagus, stomach, duodenum and small intestine. No stenotic lesion was seen in any part of the gastrointestinal tract. The pneumoperitoneum disappeared three weeks after admission.

Follow-up examination one year after discharge showed a well-nourished man with no complaints. Flat roentgenograms of the abdomen showed a rather unusual quantity of air in the stomach and small intestine without fluid levels. No pneumoperitoneum was seen.

Comment. This undernourished patient under emotional stress due to his recent arrival in the country was admitted with a marked pneumoperitoneum. No signs or symptoms of peritoneal inflammation were present and, therefore, the abdomen was not explored. No ulcerative and/or stenotic lesion was found on subsequent roentgenologic examination of the gastrointestinal tract. The pneumoperitoneum disappeared three weeks after admission upon improvement of his physical condition.

Re-examination a year later showed a well-nourished happy man.

DISCUSSION

The 4 above-described cases have many common features, but show some different findings as well.

The most evident common findings in all cases were pneumoperitoneum, malnutrition and vomiting, on one hand, and absence of signs of an acute abdomen, on the other. The pneumoperitoneum disappeared gradually on conservative treatment in all patients. In our opinion the disappearance of the pneumoperitoneum was due to the improved nutritional state.

The severe malnutrition in the first 3 cases is well explained by the long-standing marked pyloric obstruction. In the fourth patient the malnutrition was probably due to his emotional stress and physical strain. Reports dealing with pneumatosis intestinalis cystoides in association with a stenotic lesion of the gastrointestinal tract nearly always mention that the patients were in a poor nutritional state.[1,2,5,9,11,13,14,16,17,18] In a previous report from this hospital, a case of pneumatosis intestinalis cystoides with severe malnutrition was described.[6,15] We believe, therefore, that pneumatosis intestinalis cystoides of the described type is most probably due to malnutrition.

As we were reasonably certain that im-

mediate surgical intervention was not indicated, it was decided to prepare the patients for elective surgery by treatment aimed primarily at improving their nutritional state. All cases responded well to this treatment; the pneumoperitoneum diminished markedly or disappeared, the number of cysts became smaller and the gas in the stomach wall nearly disappeared. The complete disappearance of the cysts after gastroenterostomy also supports our opinion. Gastroenterostomy, by allowing normal food intake, removes the cause of malnutrition which, in turn, results in the disappearance of the cysts. After functional correction of pyloric obstruction, this has been observed by other authors as well.[1,2,4,5,7–10,17]

Follow-up examinations of the 3 operated cases showed that the patients remained in good nutritional state and neither the pneumoperitoneum nor the cysts recurred during a period ranging from one to three years. We have had under observation for four years another patient, severely malnourished, with pyloric obstruction and pneumatosis intestinalis cystoides who refused surgery.[15] The typical findings of pneumatosis intestinalis cystoides were present on repeat examinations, proving that this process persists as long as malnutrition is not corrected.

The rewarding results of the treatment given to our patients show that preoperative conservative therapy is indicated and that elective surgery should consist of relieving the obstruction. The cyst-bearing loops may be left alone. In Case II, volvulus of the cyst-bearing small intestinal loops and adhesions between these loops and the diaphragm were present. Though the involved loops were edematous and covered by numerous large cysts, no resection was carried out. The presence of even very numerous and/or large cysts is not an indication for resection.

The diagnosis of pneumatosis intestinalis cystoides should be made without difficulty by roentgenologic examination in typical cases. The clinician, however, can suspect the diagnosis when a pneumoperitoneum is detected in a malnourished patient, who is not acutely ill. In addition, the history of a long-standing duodenal ulcer makes the diagnosis probable. Flat roentgenograms of the abdomen in erect and supine positions show the pneumoperitoneum, the interposition of the small intestine between the liver and the diaphragm and the delicate ring shadows representing the cysts in the typical cases. In Case III, the roentgenographic finding of air in the gastric wall, without the usual appearance of cysts, was surprising. The pneumoperitoneum and the known long-standing pyloric obstruction suggested the diagnosis of pneumatosis intestinalis cystoides. We believe, therefore, that the gas in the gastric wall is equivalent to cysts on the intestines seen in other cases. To our knowledge this is the first case in which pneumatosis of the stomach presented itself in the form of a continuous intramural layer of air without cyst formation. Isolated cases of cysts on the stomach with pneumatosis of the small intestine, however, have been described.[2,7]

Case IV had only two signs in common with the first 3—pneumoperitoneum and malnutrition. Such isolated cases have been reported as idiopathic pneumoperitoneum. The pneumoperitoneum in this patient disappeared spontaneously upon rest and improvement of his nutritional state, and reappeared again with malnutrition. We believe, therefore, that this case has some relationship to pneumatosis intestinalis cystoides.[6]

As stressed above, this paper deals with pneumatosis of the benign type seen in adults only. We believe that this type of pneumatosis is due to malnutrition. This conception is supported by the following facts: (1) pneumatosis of this type is always associated with malnutrition; (2) it disappears shortly after correction of the deficient nutritional state; and (3) it perseveres with persistent malnutrition.

SUMMARY

1. Two typical, one atypical and one probable case of pneumatosis intestinalis cystoides are described. All are associated with malnutrition.

2. After correcting the malnutrition by conservative and surgical treatment, the pneumatosis disappeared.

3. The cyst-bearing parts of the gastrointestinal tract do not require resection even in cases with extensive pneumatosis because the cysts disappear spontaneously.

4. In one case the cysts completely disappeared eight days after surgery—the shortest time so far observed.

5. A hitherto unreported type of intramural gastric pneumatosis without cyst formation is described.

6. The so-called idiopathic pneumoperitoneum has probably some relationship to pneumatosis intestinalis cystoides.

7. We believe that malnutrition is the main etiologic factor of this type of pneumatosis intestinalis cystoides.

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GAS IN THE PORTAL VENOUS SYSTEM*

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THE presence of gas in the intrahepatic branches of the portal vein during life is a little known and seldom recognized condition of grave prognostic significance. It is readily detectable roentgenologically, the intravascular gas producing a branching linear pattern. As will be shown, this pattern can be distinguished from that of gas in the biliary tract.

On reviewing the literature between 1922 and 1960, we were able to find only two articles dealing with this subject. The first of these, by Wolfe and Evans[6] in 1955, reported the condition in 6 infants, ranging in age from fifteen days to six months, who were suffering from a variety of diseases. The second, by Susman and Senturia[4] in 1960, included an additional patient, an adult with mesenteric infarction, in whom the gas was detectable roentgenographically and confirmed at operation.

We have encountered 4 patients with gas in the portal system at the Cincinnati General and Children's Hospitals during the past three years. In 3, the classic roentgen features were evident. In the fourth, roentgenograms were not available, the gas being found at autopsy. In one of the cases (Case 1), the nature of the gas and its pathogenesis have been established with reasonable certainty.

REPORT OF CASES

CASE 1. W.W., a sixty-three year old white man, entered the Cincinnati General Hospital on July 21, 1960, with a six hour history of severe abdominal pain, distention, and diarrhea. He had been on peptic ulcer management because of a prior history of postprandial pain and two episodes of tarry stools, the last of which had occurred six months earlier.

Physical examination revealed a temperature of 96.5° F. and a pulse of 130. Positive findings were limited to the abdomen, which was distended and tympanitic. Following gastric aspiration of three liters of thick foul brown fluid and air, the distention subsided and the abdomen became soft and nontender. On rectal examination a large amount of bright red watery stool was noted. Sigmoidoscopy was normal.

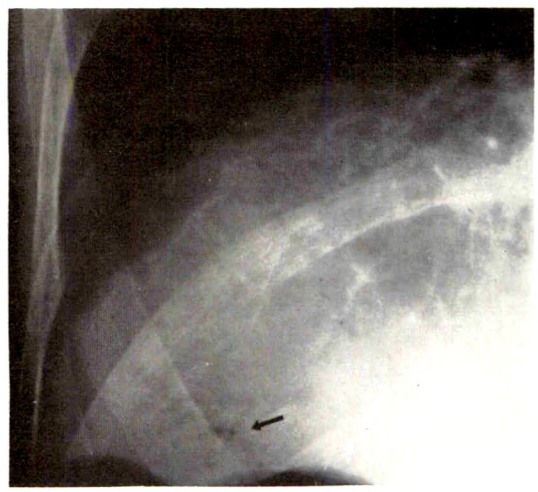


FIG. 1. Case 1. Detail view of the liver area on admission showing a few branching linear gas shadows (arrow) near the periphery of the right lobe.

Laboratory studies revealed a hemoglobin of 12 gm. and a white blood cell count of 12,300 per cu. mm., with 80 per cent neutrophils. The blood urea nitrogen, CO_2 combining power, and serum amylase were normal. The blood chloride was slightly decreased, and the blood sugar was 253 mg. per cent. The clotting time was slightly prolonged but the bleeding and prothrombin times and platelet count were normal.

Recumbent and upright roentgenograms of the abdomen showed marked distention of the stomach and moderate distention of the small bowel with multiple gas-fluid levels. Within the confines of the liver shadow were several small branching linear gas shadows (Fig. 1). It was felt that they represented gas in the portal system, probably secondary to necrosis of the

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bowel. Roentgenograms made the following day no longer showed these branching shadows. Barium enema examination was normal.

Exploratory laparotomy was performed two days after admission. Marked distention of the small bowel hampered the procedure. One member of the surgical team thought that a 180° volvulus of the small bowel was present, but another disagreed. A ten inch segment of partly gangrenous ileum, lying about four feet proximal to the ileocecal valve, was resected.

Postoperatively, the patient improved considerably. Although the diarrhea persisted, it was no longer bloody. Five days after the operation the patient suddenly went into shock and complained of severe abdominal pain. Portable roentgenograms of the abdomen revealed free intraperitoneal air, small bowel distention, and two segments of edematous bowel in the right lower quadrant. No gas was visible in the hepatic vessels. Stool guaiac test was 4 plus. Blood culture revealed abundant *Aerobacter aerogenes*. The patient remained in shock, became markedly oliguric and acidotic, and died the following day. The body was taken immediately to the radiology department where an abdominal roentgenogram was obtained (Fig. 2, *A* and *B*). This revealed extensive gas in the portal veins and in several mesenteric veins. In addition, there was considerable gas in the extraperitoneal space adjacent to the bladder, in the wall of several segments of intestine, and in the abdominal wall.

At autopsy marked crepitation of the abdominal and thoracic parietes, neck, and scalp was noted. Free peritoneal gas was found. Gas was visible in the mesenteric, portal, hepatic, and jugular veins, in vessels at the base of the brain, in the right atrium, and in the abdominal wall, extraperitoneal space, serosa of the bowel, and mesentery. Before dissection was carried out, gas was withdrawn from the portal and jugular veins and the right atrium by a vacuum syringe. It was felt that some contamination of the syringes with room air probably occurred.

The peritoneal cavity contained 2,500 cc. of cloudy light brown fluid. The mesenteric vessels were normally patent. Enteric contents leaked from the site of anastomosis. The intestines, especially the distal colon, showed intense congestion, hemorrhage, and areas of necrosis. The stomach showed similar findings and, in addition, a large chronic active prepyloric ulcer which had penetrated into the pancreas. The gallbladder and bile ducts were normal. All vessels leading to and from the liver were ligated prior to its removal. A roentgenogram

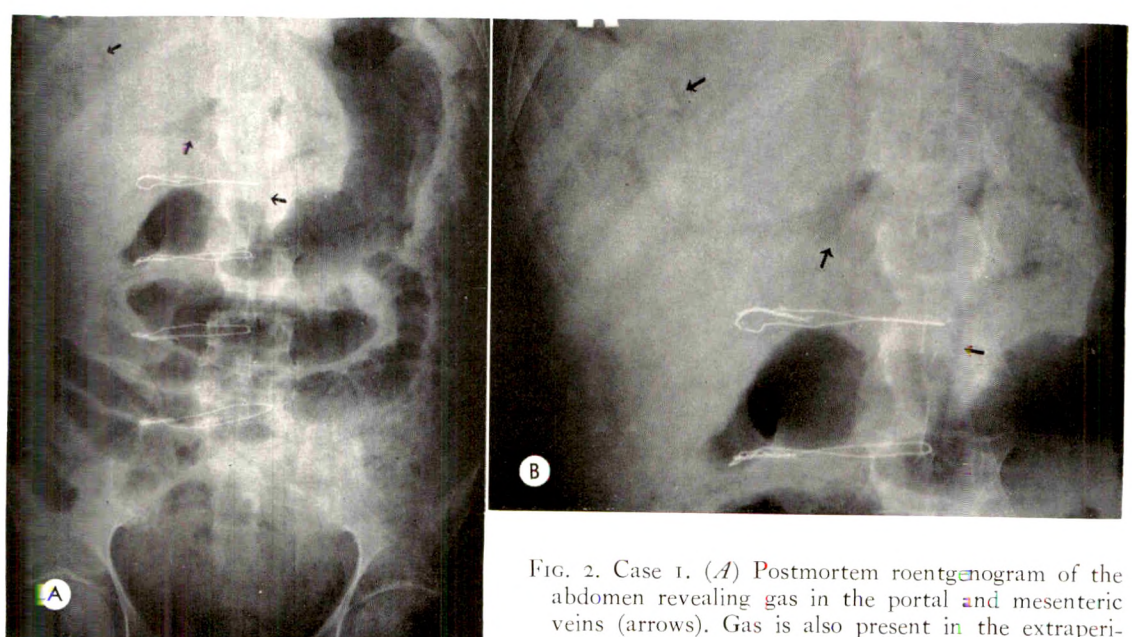


FIG. 2. Case 1. (*A*) Postmortem roentgenogram of the abdomen revealing gas in the portal and mesenteric veins (arrows). Gas is also present in the extraperitoneal space in the region of the bladder and in the wall of several segments of intestine in the left lower quadrant. (*B*) Enlargement of upper portion of *A*. A large mesenteric vein (lower arrow), the portal vein (middle arrow), and its intrahepatic branches (upper arrow) are seen.

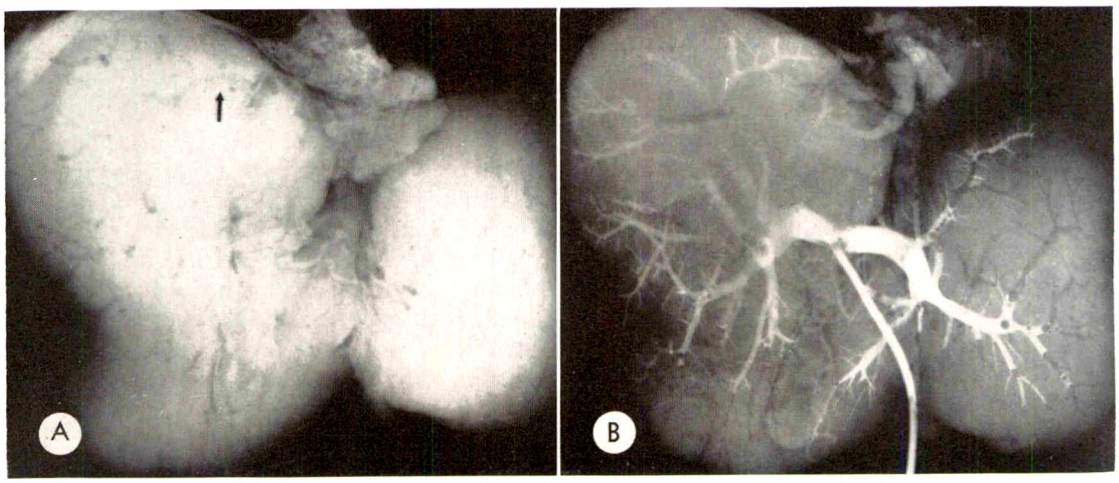


Fig. 3. Case I. (*A*) Roentgenogram of the liver removed after ligation of vessels at autopsy. Gas is seen within the portal veins and in at least one large hepatic vein (arrow). (*B*) Roentgenogram of the liver following the injection of barium into the portal system demonstrating the location of the gas. A later injection of the hepatic veins confirmed the location of the gas near the dome of the liver.

of this organ revealed considerable intravascular gas (Fig. 3*A*), some of which was withdrawn with an oiled needle and syringe. Barium was then injected into the main portal and hepatic veins, and a roentgenogram showed that most of the gas lay in the portal branches with a small amount in a large hepatic vein (Fig. 3*B*).

Microscopic sections of the colon, small bowel, and stomach showed hemorrhage, congestion, and necrosis. A large number of bacteria was visible in the sections. Several large spaces were seen in the submucosa of the stomach. Clusters of bacteria were present in the wall of the aorta and in small arteries and lymphatics in some of the viscera.

Cultures of the blood, lung, bowel, liver, and peritoneal fluid showed an abundant growth of *Aerobacter aerogenes*, interspersed with a few colonies of *Staphylococcus aureus* and *Streptococus alpha-hemolyticus*. The gas analyses yielded 24 per cent CO_2 in the gaseous phase in the liver, 28 per cent in the portal vein, 38 per cent in the jugular vein, and 35 per cent in the right atrium. The final pathologic diagnosis was acute hemorrhagic necrotizing gastroenterocolitis[2,5] and *Aerobacter aerogenes* septicemia.

Comment. A sixty-three year old man entered the hospital with acute abdominal symptoms and bloody diarrhea. Abdominal roentgenograms showed gas in the hepatic vessels and distention of the stomach and small bowel. Exploratory laparotomy revealed a necrotic segment of small bowel. Five days postoperatively he went into shock and died. A postmortem roentgenogram of the abdomen revealed extensive intravascular and interstitial gas. At autopsy, gas was present in the mesenteric, portal, and jugular veins and in the heart. The bowel showed acute hemorrhagic necrotizing gastroenterocolitis. Both antemortem and postmortem blood cultures grew *Aerobacter aerogenes*. Analysis of the gas revealed a high content of carbon dioxide.

Case II. R.A., a thirty-five year old Negro male, was admitted to the Cincinnati General Hospital on June 21, 1958, comatose and in shock. He was a known diabetic and had taken his insulin the day prior to admission. While driving from Alabama with several companions, he became "car-sick" and ingested nothing but ice water and orange juice for twenty-four hours. On the following morning he could not be awakened and was brought to the hospital.

The temperature and pulse were normal but the respirations were 28 per minute. The blood pressure could not be obtained. Physical examination revealed anisocoria, absence of corneal reflexes, hypoactive tendon reflexes, and marked abdominal distention without audible bowel sounds.

The blood urea nitrogen was 84 mg. per cent and the sugar 854 mg. per cent. The CO_2, blood chlorides, and pH were extremely low. There was 4 plus glycosuria with moderate acetonuria. The stool guaiac test was negative.

Recumbent and decubitus roentgenograms of the abdomen (Fig. 4, *A* and *B*) revealed gaseous distention, severe in the small bowel and moderate in the ascending colon, with an occasional fluid level. Many slender, branching, linear gas densities were visible within the right side of the liver, increasing somewhat in caliber as they converged toward the hilus, but not reaching the size of a major vessel or duct. There was no gas in the gallbladder or extrahepatic biliary ducts. At first an internal biliary fistula was suspected, but subsequently a diagnosis of portal vein gas was made.

Despite supportive measures, including vigorous treatment of the diabetic acidosis, the patient expired eight hours after admission.

Autopsy was performed forty-eight hours post mortem, so a blood culture was not obtained. The small bowel was quite distended and its mucosa showed marked congestion but no evidence of ulceration or necrosis. No mention was made of intramural or intravascular gas, the prosector having had no knowledge of the roentgen findings. The stomach, colon, gallbladder, and biliary ducts showed no abnormality. The mesenteric vessels appeared normal. The liver was grossly normal and microscopically showed only mild congestion. With the exception of marked pulmonary edema, no other significant abnormalities were noted. The cause of death was listed as diabetic acidosis.

Comment. A diabetic entered the hospital in shock and acidosis and died eight hours later. Roentgenograms revealed intravascular gas in the liver and severe nonobstructive ileus. At autopsy the small bowel showed marked distention and mucosal congestion.

Case III. J.A., a Negro female aged fifty-two, a diabetic of at least eleven years' duration, was admitted to the Cincinnati General Hospital on December 5, 1957, with a four day history of lower abdominal pain, diarrhea, and vomiting. She had eaten very little during the current illness but had taken 20 units of insulin per day. Bilateral supracondylar amputations of the lower extremities had been performed about ten years earlier. She had been blind for one year.

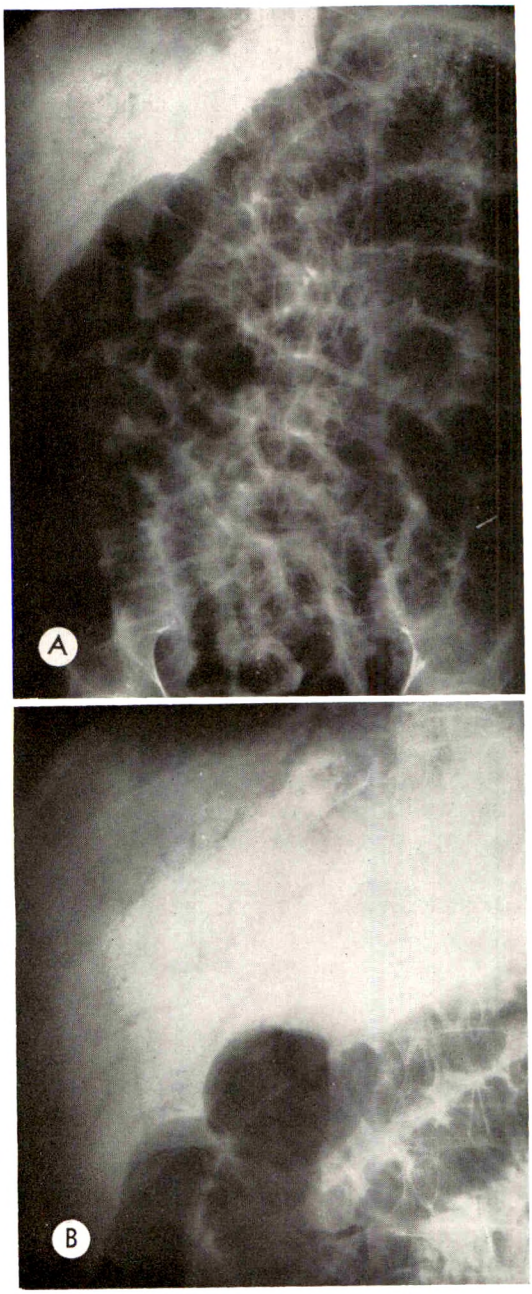


Fig. 4. Case II. (*A*) Recumbent roentgenogram revealing extensive gaseous distention of the intestines. Branching linear gas shadows are visible within the right side of the liver. (*B*) Detail view of the liver area.

On admission the blood pressure was 215/105. The temperature was normal but the pulse was 104. She was drowsy but coherent. The

abdomen revealed hyperactive bowel sounds and diffuse tenderness.

The white blood cell count was 29,000 with 86 per cent neutrophils. The urine showed 2 plus sugar, 1 plus acetone, and 4 plus albumin. The blood urea nitrogen was 42 mg. per cent and the blood sugar 253 mg. per cent. The CO_2 and blood chlorides were slightly decreased. The stool was positive for occult blood.

Flat and decubitus roentgenograms of the abdomen revealed a few slightly dilated loops of small bowel. The following day the patient's general condition worsened. Abdominal roentgenograms now revealed marked small bowel distention with many fluid levels. Several thin linear gas shadows were visible in the right lower quadrant, apparently lying in intestinal wall or mesenteric vessels. Within the confines of the liver shadow, a few thin, faint, bifurcating, linear gas shadows were noted. Several small gas bubbles were present in the right flank (Fig. 5, *A* and *B*).

Although mesenteric infarction was suspected from the time of admission, the condition of the patient precluded operation, and she died forty hours after admission and four hours following the final roentgenograms.

Autopsy was performed nine hours after death. The prosector noted the presence of gas within vessels in the neck but made no mention of gas within the liver, mesenteric vessels, or gut wall. The small bowel was greatly distended with fluid and gas. Its mucosa appeared swollen and markedly congested. The superior mesenteric artery was occluded about 7 cm. from its origin by a dry firm thrombus. The colic branches arose proximal to the occlusion. The colon, liver, gallbladder, and biliary ducts appeared normal.

Microscopic examination of the small bowel revealed many areas of necrosis. The liver showed pericentral congestion and occasional cellular necrosis but no evidence of inflammation. Postmortem blood culture yielded *Proteus mirabilis*, *Proteus aerogenoids* and *Clostridium paraputrificans*.

Comment. This diabetic female had mild acidosis and acute abdominal symptoms. Intravascular gas in the liver, marked small bowel distention, and linear gas shadows lying either within mesenteric vessels or the intestinal wall were seen roentgenographically a few hours before death. Autopsy revealed gas within vessels in the neck, and small bowel necrosis secondary to mesenteric artery thrombosis. Postmortem blood culture yielded three different gas-producing organisms.

Case iv. D.I., a one day old boy, entered Children's Hospital with evidence of esophageal atresia. Two days later this was corrected surgically. The subsequent course was stormy and he expired on the sixth postoperative day. At autopsy gas was found in all chambers of the

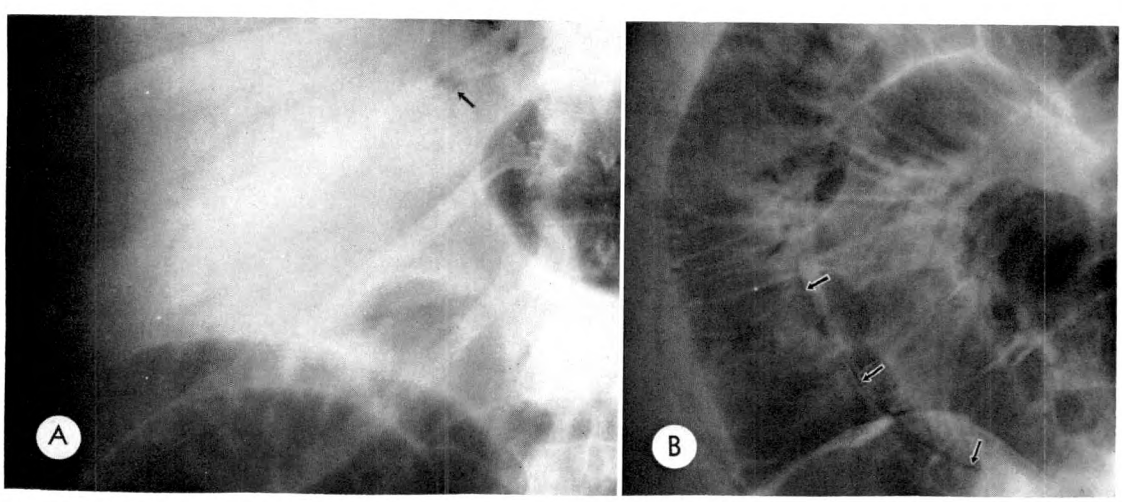


Fig. 5. Case iii. (*A*) Enlarged view of liver area revealing a few bifurcating linear gas shadows (arrow). (*B*) Roentgenogram of right midabdomen showing a long linear gas shadow (arrows) lying either in the intestinal wall or in a mesenteric vessel. A small gas bubble is visible in the flank.

heart, in the inferior vena cava, in the portal vein, and in the intercostal arteries. The intestinal tract appeared normal. *Aerobacter aerogenes* was cultured from the blood. Microscopically, numerous bacterial colonies were seen in the liver. The final pathologic diagnosis was *Aerobacter* septicemia, pneumonia, and purulent mediastinitis.

DISCUSSION

In addition to the 4 cases described, one of us (B.F.) has seen 2 others with gas in the hepatic vessels. Unfortunately, this was over ten years ago and the patients' names have been lost, so that the roentgenograms and hospital records are not available for review. The first of these was a middle-aged man who entered the Dayton Veterans Hospital with signs and symptoms of small bowel obstruction. Roentgenograms of the abdomen revealed branching linear gas shadows within the liver and evidence of small bowel obstruction. At operation a closed loop small bowel obstruction with intestinal necrosis was found. The patient died postoperatively. Autopsy was not performed. The second case was that of a newborn infant who showed roentgen evidence of small bowel obstruction and gas within the hepatic vessels. The infant died without operation. Autopsy was not done. Because of limited information, these 2 cases were excluded from the present series.

Table 1 is a summary of the findings in the 11 recorded cases of intravascular gas in the liver, including the 4 in the present report. There were 7 infants and 4 adults. Nine were males. Only 2 were diabetic, both in the present series.

Antemortem blood culture was recorded in 2 cases, one being negative and the other showing *Aerobacter aerogenes*. In 9 of the 11 cases, postmortem blood cultures were performed and all were positive, *E. coli* being found in 6, *Aerobacter aerogenes* in 2, and *Clostridium paraputrificans* and two types of *Proteus* in 1. All of the *E. coli* cultures were encountered in Wolfe and Evans' series of infants, and both of the *Aerobacter* cultures were from our own series, one in an adult and the other in an infant.

Marked distention of the gut, shown roentgenographically or pathologically, was present in 10 of the cases. Although in every instance the intrahepatic gas was believed to lie within the portal system, in 5 cases it was actually visualized in the portal vein at autopsy. It was also recognized pathologically in mesenteric veins in 7 cases, in the inferior vena cava in 2, in a jugular vein in 2, in a hepatic vein in 1, in iliac and intercostal arteries in 1 each, in vessels at the base of the brain in 1, and in one or more cardiac chambers in 3. In addition, gas was demonstrated in the gut wall in 5 cases, pathologically in 4 and roentgenographically in 2.

All of the 8 patients who had roentgenograms showing intravascular gas died soon thereafter, only 2 surviving more than twenty-four hours. These died seven and eight days, respectively, after the first roentgen evidence of the gas.

The underlying diagnoses in the cases reported included, among others, 3 cases of erythroblastosis fetalis, 2 of mesenteric infarction, 2 of diabetes mellitus, 2 of necrotizing enterocolitis, and 1 each of imperforate anus, duodenal atresia, and esophageal atresia. Diarrhea occurred in 5 of the infants and 1 of the adults.

In searching among these cases for a common denominator which might explain the presence of gas in the vascular system, some interesting factors come to light. In the first place, all the organisms found on antemortem and postmortem blood cultures in these cases are potential gas-formers, especially in the presence of sugar. This raises the possibility of sepsis, at least in the portal circulation, as the cause of the gas. The well-known association of diabetes and gas-producing infection underscores the importance of the diabetes in Cases 11 and 111, and lends support to an infectious etiology of the intravascular gas.

The bacteria isolated in the blood cultures are all inhabitants of the normal intestinal tract. Necrosis of bowel wall, present in at least 4 of the 11 cases, certainly might predispose to their invasion

TABLE I

Author	Age	Sex	Diabetes	Blood Culture		Distention of Gut	Gas Other Than in Liver	Survival after Recognition of Gas	Other Diagnoses	Confirmation of Intravascular Gas
				Antemortem	Postmortem					
Wolfe and Evans[6]	17 da.	M	○	Negative	E. coli	+	Mesenteric veins; inferior vena cava; right atrium; wall of small and large intestine	15 hr.	Imperforate anus; pneumonia	Roentgenograms and autopsy
Wolfe and Evans	35 da.	M	○		E. coli	+	Mesenteric veins	7 da.	Duodenal atresia; postoperative intestinal obstruction; necrotizing enteritis	Roentgenograms and autopsy
Wolfe and Evans	15 da.	M	○		E. coli	+	Mesenteric veins; wall of large intestine	6 hr.	Erythroblastosis fetalis; cerebral vascular thrombosis; bronchopneumonia	Roentgenograms and autopsy
Wolfe and Evans	16 da.	M	○		E. coli	+		14 hr.	Erythroblastosis fetalis; bilateral renal cortical necrosis; pulmonary edema	Roentgenograms and autopsy
Wolfe and Evans	3 mo.	F	○		E. coli	+	Mesenteric veins; iliac arteries; wall of duodenum and jejunum		Diarrhea	Autopsy only
Wolfe and Evans	19 da.	M	○		E. coli	+	Mesenteric veins		Erythroblastosis fetalis; aspiration pneumonia; acute gastroenteritis	Autopsy only
Susman and Senturia[4]	77 yr.	M	○			+	Mesenteric veins	24 hr.	Superior mesenteric artery thrombosis	Roentgenograms and operation
Wiot and Felson Case I	63 yr.	M	○	Aerobacter aerogenes	Aerobacter aerogenes	+	Mesenteric, hepatic and jugular veins; right atrium; intestinal wall; extraperitoneal space; abdominal wall; mesentery; vessels at base of brain	8 da.	Acute necrotizing hemorrhagic enterocolitis; septicemia	Roentgenograms and autopsy
Wiot and Felson, Case II	35 yr.	M	+			+		8 hr.	Diabetic acidosis	Roentgenograms only
Wiot and Felson, Case III	52 yr.	F	+		Proteus; Clostridium	+	Cervical vessel (probably jugular vein); probably intestinal wall	4 hr.	Superior mesenteric artery thrombosis; diabetes	Roentgenograms and autopsy
Wiot and Felson, Case IV	6 da.	M	○		Aerobacter aerogenes	○	Intracardiac; inferior vena cava; intercostal arteries		Esophageal atresia; septicemia; pneumonia; purulent mediastinitis	Autopsy only

of the portal system. Unfortunately, the general unreliability of postmortem cultures lessens somewhat the validity of this argument. Even so, in Case 1 both antemortem and postmortem blood cultures grew abundant *Aerobacter aerogenes* and the postmortem tissues showed many bacterial colonies. *Aerobacter aerogenes* ferments various sugars to produce carbon dioxide and hydrogen.[1] Analysis of the gas collected at autopsy from the portal and jugular veins and right atrium of Case 1 showed high concentrations of carbon dioxide. The evidence for *Aerobacter* septicemia as the primary cause for the intravascular gas in this patient is, therefore, overwhelming. Case IV presents similar but less dramatic evidence of *Aerobacter* sepsis.

That septicemia from gas-producing organisms is the major factor in *all* cases of gas in the portal system cannot be implied from our present knowledge, although the uniformly fatal outcome in all the cases thus far reported suggests this possibility.

A theory is advanced by Susman and Senturia[4] that the gas from the distended intestine, under increased pressure, enters the mesenteric vessels through necrotic areas in the gut wall. This theory is supported by the recognition of "pneumatosis" in the gut wall in 5 of the 11 cases, by the severe gaseous distention of the intestine in all but one, and by the presence of enteric necrosis in at least 4 cases. Of course, these same factors would predispose to the passage of enteric organisms into the blood stream and thus also support the sepsis theory. Certainly, the theory of transmural migration of gas cannot explain the cases with intact intestinal mucosa.

It is our own belief that most, if not all, cases of intravascular gas in the liver result from gas-forming enteric organisms in the portal venous system, the intestinal distention, congestion, and necrosis probably playing an important role in the migration of the organisms through the intestinal wall.

The term "pneumatosis cystoides intestinalis," applied by Wolfe and Evans[6] to the intramural intestinal gas, is better avoided for the present, in view of its more specific connotation. We do not believe it is the instigating cause of the portal venous gas but consider it more likely the effect of a simultaneous intramural infection. The presence of gas within the hepatic veins, cardiac chambers, and peripheral veins indicates either extension of the gas, or of the organisms, through the portal capillaries.

The roentgen localization of the gas to the portal venous system and its differentiation from gas in the biliary system merit further discussion. Anatomically, the branches of the hepatic artery, portal vein, and bile duct lie together in the liver within a common sheath. Only their large extrahepatic portions show distinct differences in size, position, and direction. The hepatic veins, of course, show a completely different pattern as they enlarge and converge cephalad (Fig. 6, *A*, *B* and *C*).

There is no doubt that in all these cases the intrahepatic gas lies within the portal veins. It was actually seen within the portal system or its mesenteric tributaries in 9 of the cases, and it was clearly depicted roentgenographically in intrahepatic portal divisions in Case 1. Since the roentgen pattern of the hepatic veins bears no resemblance, the only other vascular system to be considered is that of the hepatic artery. We have been unable to find any case reports of gas within this system in the literature.

On the other hand, gas within the biliary system is more difficult to exclude. In this condition, when the gallbladder or extrahepatic bile ducts contain gas, as is usually the case, differentiation from intravascular gas is easy. If only the intrahepatic ducts show the gas, the problem becomes more troublesome. As pointed out by Susman and Senturia, however, most of the gas in the biliary tree, because of the caudal flow of bile, is found in the larger ducts. The reverse circumstances pertain in the case of gas in the portal venous system. Thus, gas seen predominantly in smaller peripheral branches is considered to lie in the portal

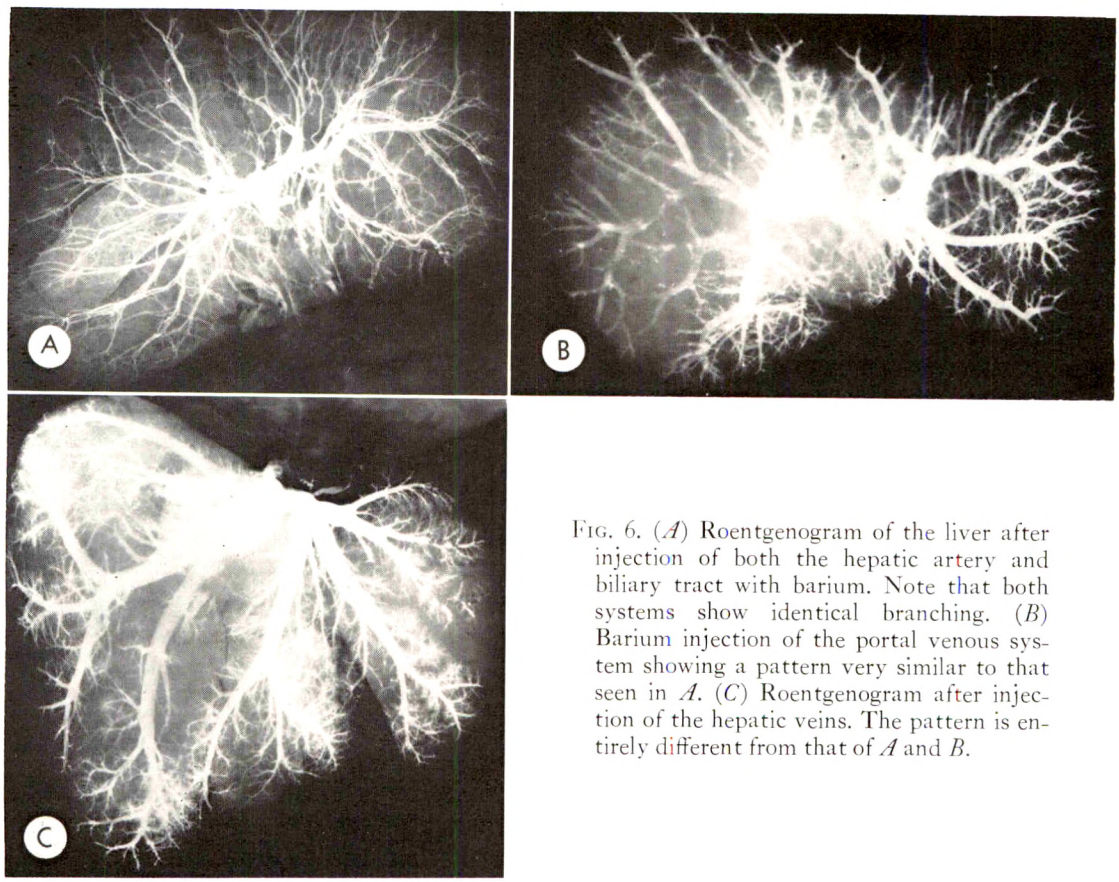


FIG. 6. (*A*) Roentgenogram of the liver after injection of both the hepatic artery and biliary tract with barium. Note that both systems show identical branching. (*B*) Barium injection of the portal venous system showing a pattern very similar to that seen in *A*. (*C*) Roentgenogram after injection of the hepatic veins. The pattern is entirely different from that of *A* and *B*.

vessels; if confined to larger, more caudal trunks, it is assumed to be in the biliary ducts. To date, this distinction has proved to be completely reliable. If doubt still exists, oral contrast medium may be used to attempt the delineation of an internal biliary fistula. On occasion, careful study of the roentgenogram will reveal gas in the mesenteric vessels or intestinal wall, as in 2 cases in the present series.

Some mention should be made of the occurrence of gas within the vascular system of the fetus, seen in cases of intrauterine death. Many explanations for this phenomenon have been offered,[3] but its pathogenesis has not been established. We do not believe that the mechanism is the same as that in the condition under discussion.

The presence of gas in the portal venous system is, at present, a sign of imminent death. All the patients have died, most within twenty-four hours. The longest survival was eight days from the time of its recognition. Whether the gas within the portal venous system is the actual cause of death or only an interesting terminal manifestation is unknown. For the present no specific therapy directed toward the intravascular gas itself is suggested. Aggressive treatment of the underlying disease and its complications (mesenteric infarction, sepsis, etc.) and, particularly, the use of those antibiotics effective against gas-forming organisms may result in the salvage of some cases in the future.

Of the 11 cases reported, 10 were seen in two institutions. This implies that the condition is considerably more common than the literature indicates, but that it is probably being overlooked. Careful examination of the hepatic region on the abdominal roentgenograms of all acutely ill patients

for these characteristic branching gas shadows will, we believe, result in the recognition of many more cases of this entity.

SUMMARY

Gas in the portal venous system presents a striking and diagnostic roentgenographic appearance which can be differentiated from gas in the biliary tree. Eleven cases, including 4 in the present series, have now been reported. The etiology has not been established, but evidence indicates that septicemia caused by gas-forming enteric organisms accounts for at least some cases. A high carbon dioxide content of the gas was established in one of the present cases. The frequency of distention, congestion, and necrosis of the intestine accompanying this condition strongly suggests an etiologic relationship. The prognosis is grave, all patients so far reported having died shortly after recognition of the intravascular gas.

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THE INTRAMURAL CYSTIC DUCT REMNANT*

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IN TEN to fifteen per cent of patients with gallbladder disease, the symptoms are not relieved or they recur after cholecystectomy. One of the causes producing the so-called postcholecystectomy syndrome is the incomplete removal of the cystic duct, leaving behind a residual stump which can give rise to symptoms similar to those of gallbladder disease. This condition has been well described in the medical literature.[5,7]

This paper deals with the study of a less frequently recognized entity consisting of the presence of a cystic duct remnant of the intramural type. This results from incomplete removal of an anomalous portion of the cystic duct which is intimately bound to and hard to separate from the common bile duct.

ANATOMIC AND EMBRYOLOGIC CONSIDERATIONS

Normally, the cystic duct is from 1 to 1½ inches long and runs from the neck of the gallbladder to join the common hepatic duct at an acute angle, forming the common bile duct. Nevertheless, Flint[4] observes that the ducts do not unite immediately but are bound together in a connective sheet, and can be separated by careful dissection for a distance of from a few millimeters to several centimeters.

In reviewing the biliary tree of 45 cadavers, the author found that 25 had a normal angular junction of the cystic and hepatic ducts. In 10 cadavers the distal segment of the cystic duct ran parallel to the common duct and both were bound together by a fibrous union for a distance of less than 1 cm. In the remaining 10 cadavers studied, the two ducts were bound firmly together for lengths of 1 cm. to 1 inch; the bound segment of the cystic duct appeared to be embedded in the medial wall of the common duct but the lumens were separate (Fig. 1, *A* and *B*). A thin septum was found between the two ducts after careful dissection of the anterior wall. The gross appearance before dissection was that of a single duct.

This is the intramural variant of the cystic duct which occurred in 22 per cent of the cadavers studied. Similar findings were reported in 1929 by Beaver,[1] who found 26 per cent of 57 cadavers having a variation of the cystic duct similar to the one described here, which he called the "short parallel type."

This variation corresponds to what Boyden[2,3] calls "septate ductus choledochus" in classifying the developmental anomalies of the extrahepatic biliary tract. Embryologically it can be explained as produced by a double vacuolization of a segment of the common duct during the solid stage of development.

In the early embryonic stage the biliary ducts appear as hollow structures which later become solid as parietal cells migrate into the lumens. These solid epithelial structures then undergo a process of vacuolization, which restores the lumen. Almost always a single row of vacuoles appears, but in some instances a double row develops and gives rise to the formation of a septate common bile duct which will have an intramural segment of the cystic duct within its medial wall.

CLINICAL CONSIDERATIONS

An intramural remnant of the cystic duct may produce no symptoms after cholecystectomy, but it can be the site of pathologic changes such as those found in cases with remnants of the gallbladder or of the

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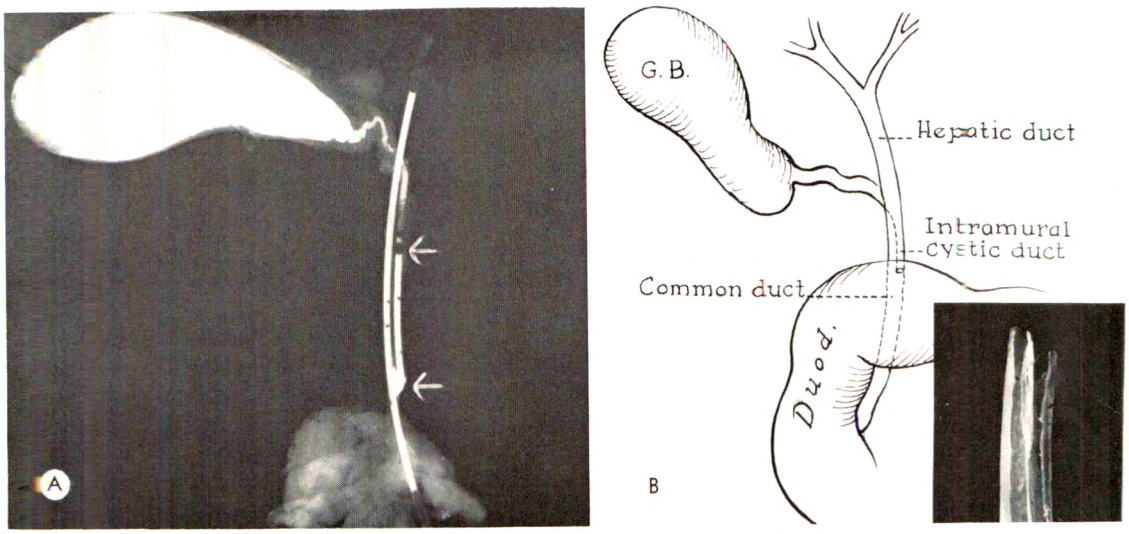


FIG. 1. (*A*) Anatomic specimen obtained from a cadaver and filled with barium. Thin polyethylene tubes were placed within the common and cystic ducts. A long intramural segment of the cystic duct measuring 1 inch in length was found running parallel to the medial aspect of the common duct (between arrows). (*B*) Diagram showing a normal biliary tree with an intramural segment of the cystic duct. The insert shows a segment of the anatomic specimen in *A* demonstrating the double lumen found at the distal portion of the common duct. The anterior wall of the duct has been dissected away. The septum separating the intramural segment of the cystic duct from the lumen of the common duct is clearly seen.

cystic duct. The symptoms may be indistinguishable from those of gallbladder disease. The need for a well-documented series of such cases is apparent in order to draw definite clinical conclusions.

ROENTGEN FEATURES

In reviewing a limited number of postcholecystectomy patients (55 cases) with studies of the biliary tree, two typical examples of an intramural cystic duct remnant were found. These will help to demonstrate the roentgen features of the condition described here. A large series will be published in the future.

The remnant of the cystic duct has been found only in the medial aspect of the common duct to date. It appears as a regular, clearly outlined segment of the distal cystic duct coursing parallel to the common duct and alongside its medial wall. The dividing septum between the remnant and the common duct can sometimes be visualized as a thin radiolucent line (Fig. 2). Nevertheless, no differentiation can be made between the two ducts at surgery.

The shadow of the intramural segment of the cystic duct may be superimposed on that of the common duct and thus may be mistaken for a normal variation of the opening of the cystic into the common bile duct (Fig. 3, *A* and *B*). These anomalies of the junction between the cystic and common ducts occur in about 10 per cent of cases,[8] and the cystic duct may open into the medial, anterior or posterior wall of the common duct.

CONCLUSION

An intramural segment of the distal portion of the cystic duct occurs more frequently than other anomalies of this portion of the extrahepatic biliary tree. Its incidence in the cadavers studied was high but apparently it does not contribute in any way to the production of gallbladder disease in the average individual. When cholecystectomy is performed and this anomaly is present, its subsequent behavior is similar to that of a cystic stump; and, if the remnant is long, dilatation ensues due to the difficulty in emptying. It may also be

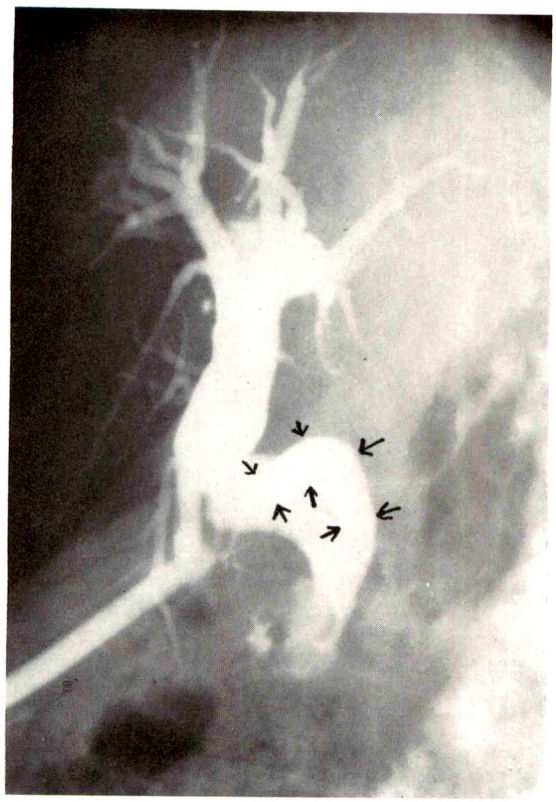


FIG. 2. T-tube cholangiogram of an elderly woman who had persisting symptoms after cholecystectomy. A second operation revealed no abnormal findings. Symptoms continued after removal of the T-tube. The intramural remnant of the cystic duct is seen in its typical medial location (arrows). Comparison with previous cholangiograms showed a progressive dilatation of the remnant, which was originally mistaken for a fistulous formation.

associated with the formation of stones, which could produce symptoms.

If this anomaly is present, postcholecystectomy studies of the biliary tree by means of T-tube or intravenous cholangiography will often demonstrate it. Serial studies may also reveal progressive dilatation or the presence of residual stones. The radiologist should be aware of this anatomic variation in order to differentiate it from other conditions, such as a common duct fistula which was suspected in the case shown in Figure 2.

Operative cholangiography will show

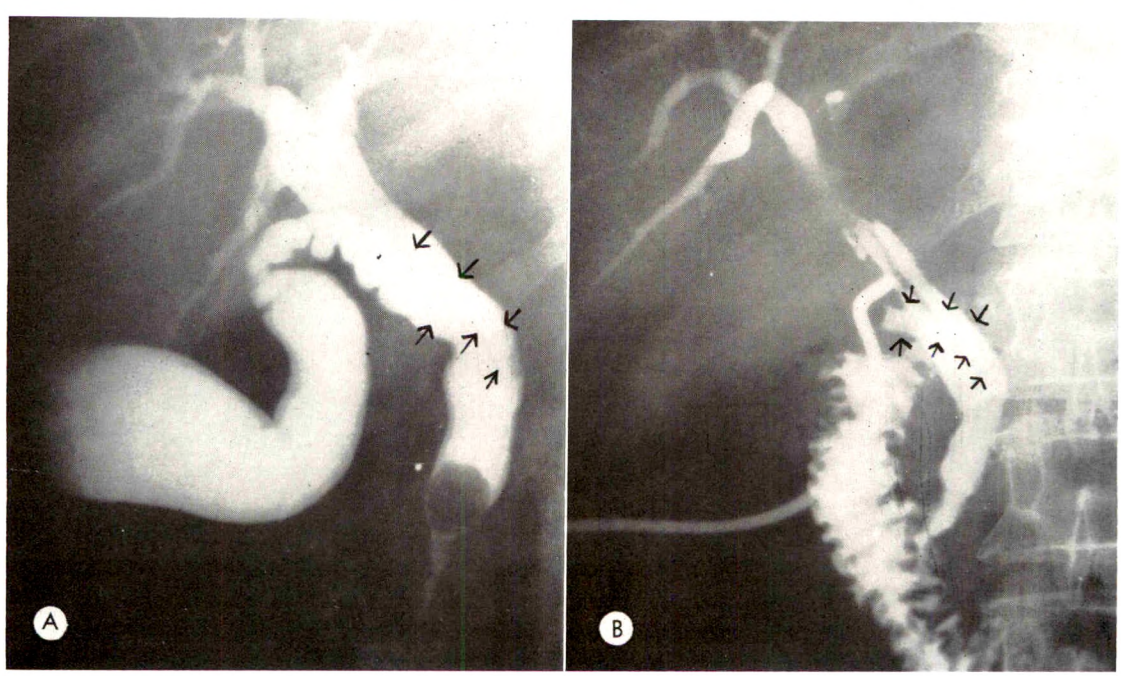


FIG. 3. (*A*) Roentgen examination of the biliary tree through a cholecystostomy. The intramural segment of the cystic duct can be seen within the projection of the common duct (arrows). There is dilatation of the biliary tree due to obstruction by the large gallstone visualized in the distal common duct. (*B*) Postcholecystectomy T-tube cholangiogram showing the intramural remnant of the cystic duct (arrows). Note its location at the medial aspect of the common bile duct.

this anomaly prior to intervening on the biliary system, especially if the contrast medium is introduced through a cholecystostomy (Fig. 3*A*). This procedure has been recommended by Hicken and coworkers[6] in order to perform an adequate cholecystectomy. Anatomic variations of the cystic duct can thus be visualized, ensuring its complete removal, if possible. Nevertheless, even after the identification of an intramural segment, its total removal may not always be accomplished by surgery. This is due to the close binding of the intramural portion of the cystic duct with the common duct.

Further evaluation of this seldom recognized condition is necessary and may be achieved in the future as newer contrast media are used for oral and intravenous studies of the biliary tree.

SUMMARY

An infrequently recognized variation of the cystic duct has been described. It consists of a short segment of the distal cystic duct which is intimately bound to the medial aspect of the common bile duct before opening into it. After cholecystectomy this segment is usually left behind and may cause recurrence or persistence of symptoms. The remnant can be identified by cholangiographic studies when the radiologist is familiar with such an anomaly of the extrahepatic biliary tree.

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CHOLEDOCHAL CYST*

REPORT OF A CASE WITH CONTRAST VISUALIZATION

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CHOLEDOCHAL cyst, a congenital localized dilatation of the common bile duct of unknown etiology, is relatively rare. Judd and Green[2] in 17,311 biliary tract operations from 1907 to 1926 encountered only 1 case of true common duct cyst. However, this pathologic condition has been known since the 18th century. According to Lavenson,[3] the first case of choledochal cyst was described by Vater in 1723.

The majority of the authors considers this condition to be congenital and Heiliger[1] reported a case in a stillborn fetus at term. It is postulated by some that the primary cause of the disease is a congenital anatomic weakness of the wall of the duct. Others feel that stenosing valve-like duplication of the wall or angulation in the distal portion of the duct plays a primary role in causing cystic dilatation. The combination of both seems most probable. Reported cysts vary in size from 1 inch to 12 inches in diameter, some occupying the entire abdomen. The distal portion of the common duct in the majority of cases is not involved. Roentgenographically, choledochal cysts have been demonstrated on plain roentgenograms as ill-defined masses in the right upper abdomen not well separated from the liver shadow. Aspiration of the cyst's contents and injection of contrast material as well as pneumoperitoneum have been done for diagnosis. Large cysts may show pressure defects on the duodenum and displacement of adjacent organs.

In 1957, Rheinlander and Bowens[6] described a case of congenital absence of the gallbladder associated with cystic dilatation of the common bile duct in which the operative cholangiogram permitted the visualization of the malformation with no contrast material passing into the duodenum. Exploration revealed a 2 cm. calculus in the left hepatic duct. Probing was unsuccessful in establishing a communication between the cyst and duodenum.

In most reported cases, oral cholecystography has failed to outline the dilated duct and rarely has the gallbladder been visualized. In 1935, Wright[8] reported a case with good visualization of the gallbladder which was displaced and deformed by a huge choledochal cyst. The cyst was not opacified by the contrast material. In 1957, Moseley[5] described a case of choledochal cyst visualized by oral cholecystography using telepaque as a contrast medium. In this case, both the gallbladder and the common duct cyst were well demonstrated. A gastrointestinal series following cholecystography showed the duodenum to be displaced, anteriorly and inferiorly, by the opacified cyst. These findings were confirmed by exploratory laparotomy. From a review of the literature, this is apparently the first report of roentgenographic demonstration of a choledochal cyst by oral cholecystography. In 1958, Liebner[4] reported the opacification of a choledochal cyst and gallbladder in an eight and one-half year old girl by both oral cholecystography and intravenous choledochography. Surgical exploration confirmed the roentgen findings.

Because of the rarity of contrast visualization of choledochal cysts, the following case seemed worthy of reporting.

REPORT OF A CASE

The patient, a twenty year old Negro female, was admitted to the Buffalo General Hospital on October 4, 1959 with a chief complaint of

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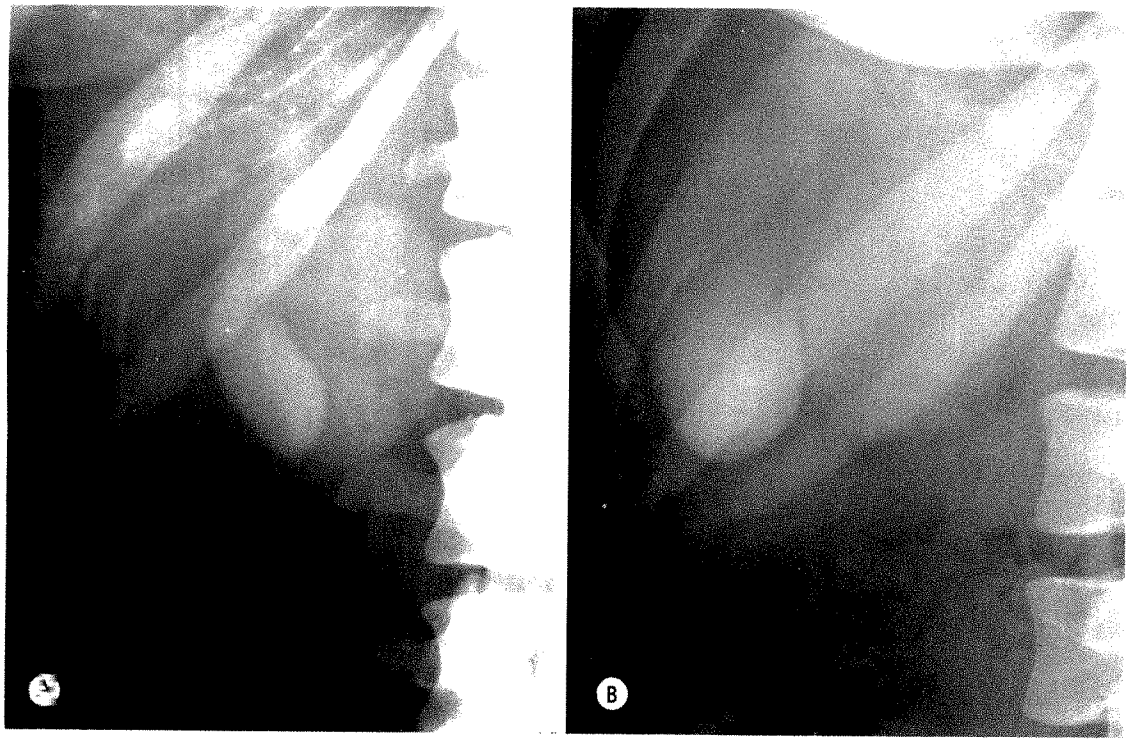


FIG. 1. Oral cholecystograms in (*A*) prone and (*B*) oblique projections.

right upper abdominal pain of four hours' duration associated with nausea and vomiting. Since the age of thirteen she had had intermittent attacks of abdominal pain classified by her as "stomach trouble." At the onset, when she was thirteen years of age, she underwent an appendectomy for these complaints. About two years prior to the present admission she had developed repeated attacks of right upper abdominal pain for which she was seen in the outpatient clinic. There had been two admissions to the hospital for pregnancy, one in March, 1958, and the second in September, 1958. Also she had been readmitted to the hospital after her first delivery because of severe right upper abdominal pain. She had multiple roentgenographic examinations which will be discussed later.

Physical examination on admission was not remarkable except for marked right upper abdominal tenderness. There was no spasm or rebound and no masses were palpated. All laboratory studies were negative. There was no evidence of clinical or chemical jaundice.

Roentgen Findings. Oral cholecystograms (Fig. 1, *A* and *B*) taken in March, 1958, showed a well-visualized gallbladder shadow. A second cyst-like structure lying medial and posterior to the gallbladder was opacified to about the same density. The interpretation at that time was a probable "double gallbladder." Upper gastrointestinal studies including the small bowel were normal. There was no evidence of any deformities or displacement by extrinsic masses. An oral cholecystogram taken in September, 1959 revealed findings identical with those of March, 1958.

Intravenous cholangiography was done when the patient entered the hospital in October, 1959. Cholangiograms up to three hours after the injection of cholegrafin showed the hepatic ducts and the proximal 3 cm. of a markedly dilated common duct. Cholangiograms taken at twenty-four hours are shown in Figures 2, *A* and *B*, and 3. Figure 4 is a composite diagrammatic sketch of the roentgen findings. It seemed quite obvious at this time that the large opacified cyst-like structure was a choledochal cyst.

Surgical Findings. Operation on October 13, 1959 disclosed a normal gallbladder with a normal cystic duct entering a dilated right hepatic duct which appeared to end blindly, and marked cyst formation. This cyst meas-

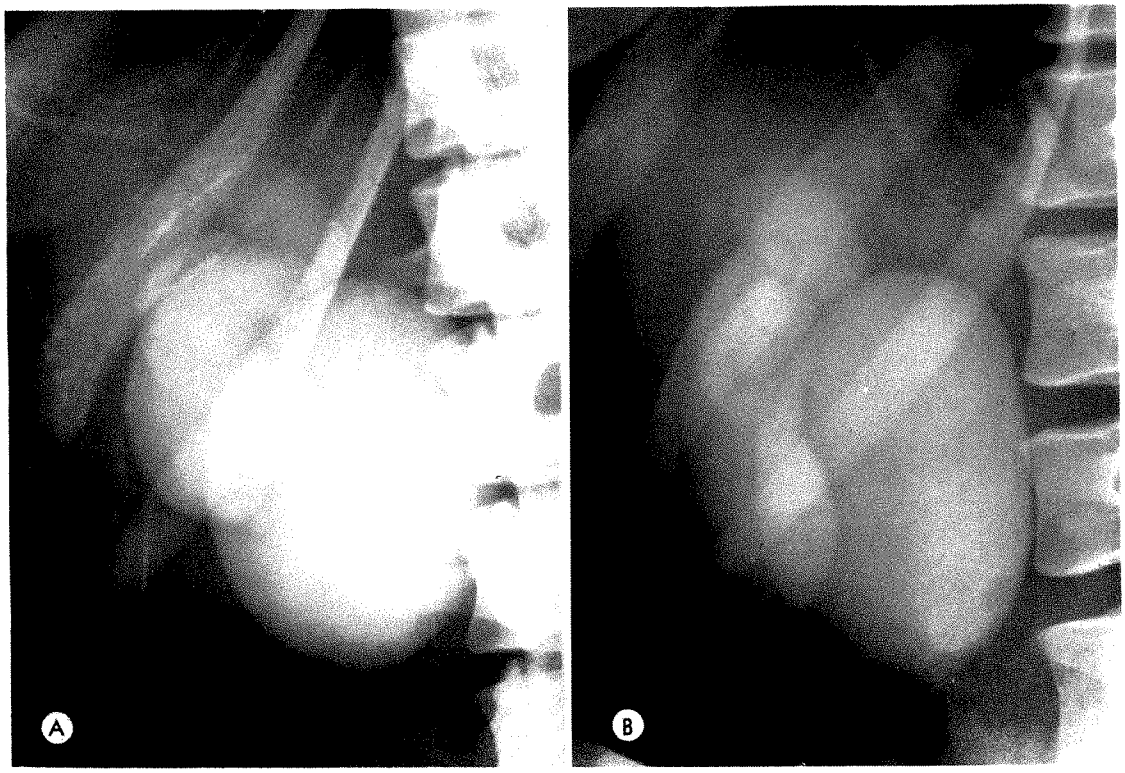
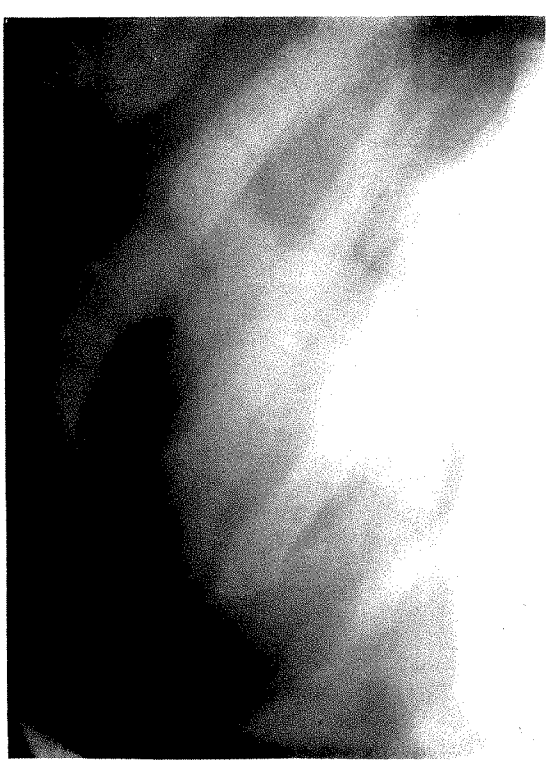


FIG. 2. Intravenous cholangiograms at twenty-four hours in (*A*) prone and (*B*) oblique projections.



ured approximately 5 inches in diameter and 300 cc. of bile was aspirated. An attempt to probe the duodenum through the cyst was unsuccessful. A normal-sized left hepatic duct was found. This had no communication with the cyst but passed downward toward the duodenum. Probing of this duct did not reveal a duodenal communication; however, it was the surgeon's opinion that such an opening did exist. (Figure 5 is a schematic drawing of the surgical findings.) An anastomosis was made between the cyst and a jejunal loop 10 inches beyond the first anastomosis. Biopsy of the cyst wall was histologically compatible with bile duct structure.

The patient's postoperative course was without complication and she was discharged to outpatient care on her tenth postoperative day. She has been relatively symptom-free since

FIG. 3. An intravenous cholangiogram in a far oblique projection shows the relation of the dilated right hepatic duct to the cystic dilatations below.

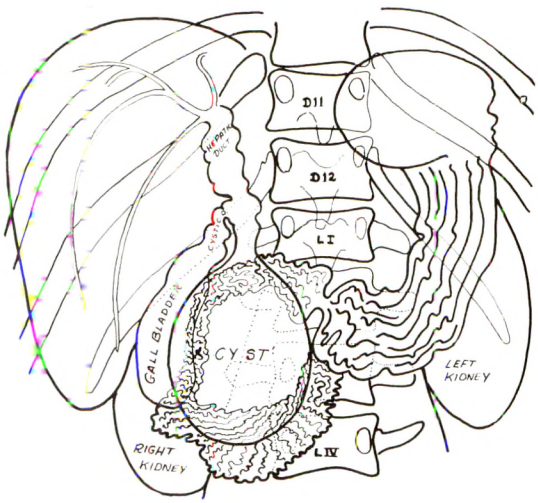


FIG. 4. Composite diagrammatic sketch of roentgen findings.

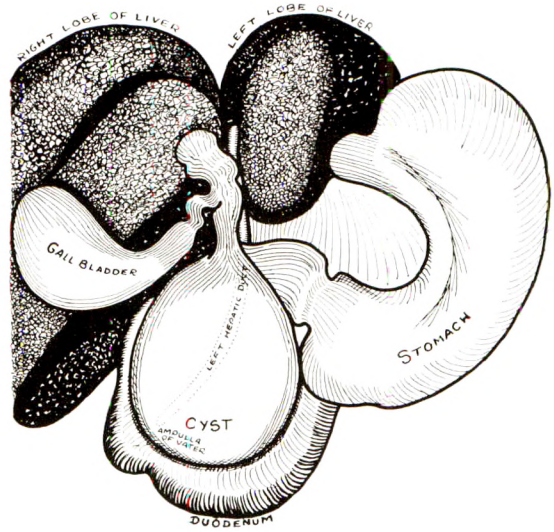


FIG. 5. Schematic drawing of the surgical findings.

surgery. She was last seen for follow-up in January, 1961.

DISCUSSION

The classic clinical triad of pain, tumor and jaundice is not always present with choledochal cysts. From a review of the literature, it is clear that frequently one component is absent and, in many instances, only abdominal pain is present. This was true in our case. At surgery frequently there is difficulty in identification and exploration of the distal bile duct. In our case it seems logical to assume that the cyst was arising from the right hepatic duct and, because of the absence of jaundice, that the left hepatic duct entered the duodenum.

Oral cholecystography is, in most instances, inadequate for demonstration of choledochal cysts. Probably, with the increased use of intravenously injected contrast media more cysts will be recognized and accurately diagnosed. Delayed filming may be of considerable importance for complete understanding of the structural changes. This was extremely helpful in the case reported here.

CONCLUSION

A case of choledochal cyst is reported which was opacified both by orally and intravenously administered contrast material. The superiority of the results using intravenous injection is stressed and it is pointed out that delayed filming may be highly important.

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THE COLLAGEN DISEASES: A DEMONSTRATION OF THE NONSPECIFICITY OF THEIR EXTRA-PULMONARY MANIFESTATIONS*

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THE broad spectrum of clinical and roentgen manifestations of the collagen diseases has been amply described.[1-6,8,9] Although the evidences of these diseases (disseminated lupus erythematosus, polyarteritis nodosa, dermatomyositis, scleroderma, rheumatic fever, and rheumatoid arthritis) are protean, each may present certain distinguishing features. However, they are often difficult to differentiate, particularly on the basis of the roentgen appearance of pulmonary involvement. We have felt, as have others, that the extrapulmonary roentgen findings in these diseases have more specificity, but more recent experience has suggested that these roentgen findings may be equally nonspecific and at times misleading.

This report is presented to illustrate these inconsistencies and to point out the broad overlap of the roentgen findings in these diseases.

REPORT OF CASES

CASE I. L.G. This thirty-four year old white woman was admitted June 3, 1958 with complaints of generalized weakness and gangrene of the right index finger. She had been hospitalized elsewhere in 1944 with a diagnosis of hemolytic anemia and had undergone splenectomy. She was readmitted to the same hospital in 1956, at which time a diagnosis of lupus erythematosus was made and confirmed by positive L.E. tests.

On her present admission, roentgen examination of the upper gastrointestinal tract showed atony and dilatation of the esophagus and small intestine (Fig. 1, *A* and *B*). Roentgen examination of the hands and wrists showed only osteoporosis. However, roentgenograms of the right forearm showed calcifications in the muscles of the proximal portion (Fig. 1, *C* and *D*).

The presence of soft tissue calcifications and the changes in the gastrointestinal tract were considered confirmatory of collagen disease and suggested scleroderma. Examination of the chest showed cardiac enlargement but no infiltration of the pulmonary parenchyma.

The patient expired shortly after admission. Autopsy confirmed the clinical impression of disseminated lupus erythematosus.

Comment: This patient with disseminated lupus erythematosus showed changes in the gastrointestinal tract and soft tissue calcifications, both of which are seen comcomly in scleroderma.

CASE II. B.J. This twenty-nine year old white woman was admitted on June 25, 1959 with complaints of weakness and fever of two months' duration. She also described intermittent dysphagia and joint pains. In May, 1959 she had been hospitalized elsewhere for evaluation and positive L.E. tests were found.

Roentgen examination of the upper gastrointestinal tract showed atony and dilatation of the esophagus (Fig. 2*A*). At fluoroscopy, the esophageal peristalsis was seen to be impaired and the distal end of the esophagus was patulous. The duodenal loop was dilated and also showed impaired peristalsis (Fig. 2*B*).

The patient's symptoms were fairly well controlled with prednisone and chloroquine but her condition gradually deteriorated and she expired approximately one year after her original admission. Autopsy showed disseminated lupus erythematosus with generalized vascular involvement.

Comment: This patient with disseminated lupus erythematosus showed changes in the gastrointestinal tract which mimicked those of scleroderma.

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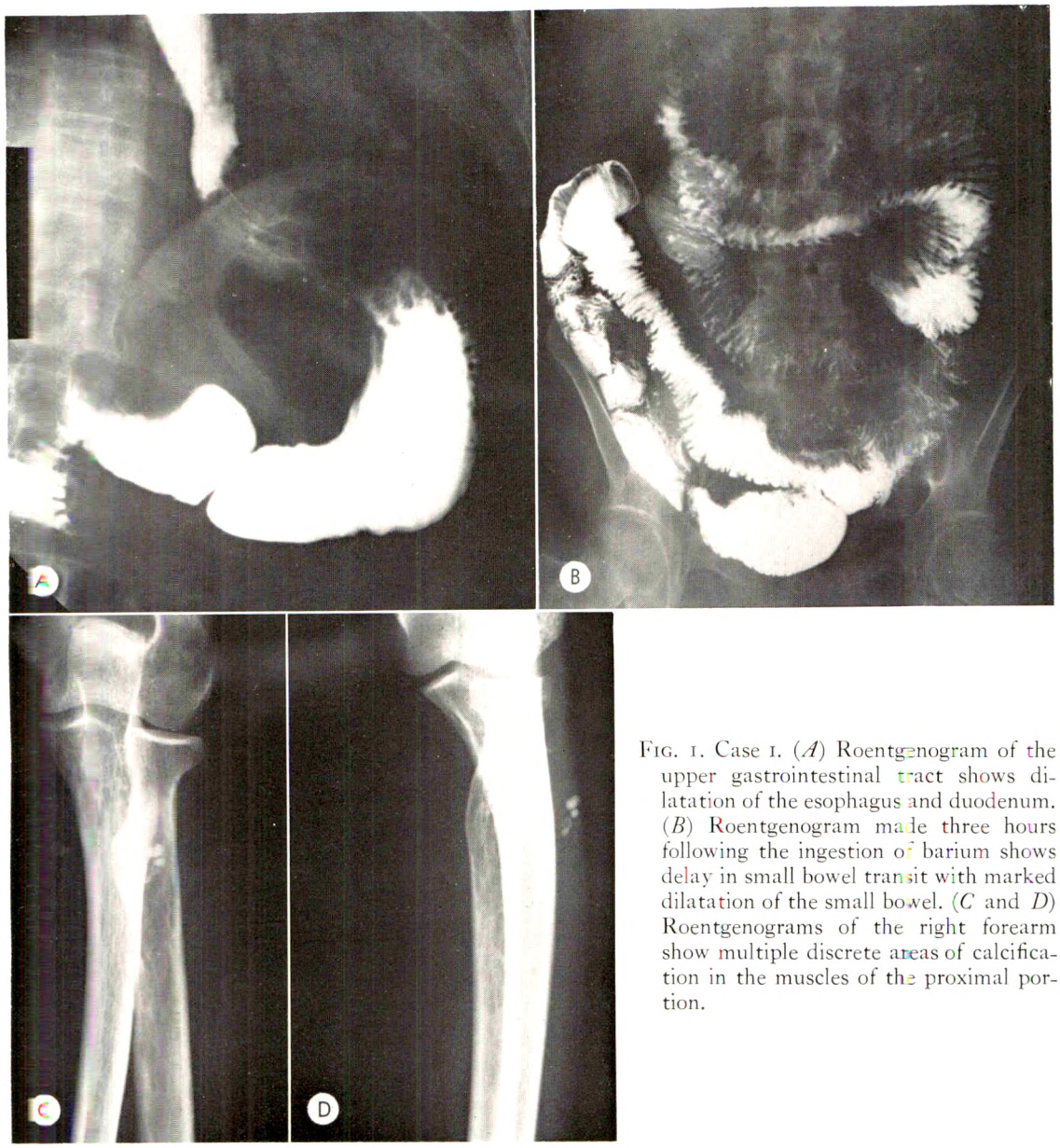


FIG. 1. Case 1. (*A*) Roentgenogram of the upper gastrointestinal tract shows dilatation of the esophagus and duodenum. (*B*) Roentgenogram made three hours following the ingestion of barium shows delay in small bowel transit with marked dilatation of the small bowel. (*C* and *D*) Roentgenograms of the right forearm show multiple discrete areas of calcification in the muscles of the proximal portion.

CASE III. J.W.B. This sixty year old man was admitted on May 15, 1958 with the complaint of ulceration of the skin of his legs. During the previous thirteen years, he had noted thickening of the skin, starting on the left hand and extending to involve the skin of the arms, chest, abdomen, legs, and feet. Four years after the onset of disease, the skin of the hands and legs broke down and became ulcerated.

Physical examination showed ulcerations of the skin of both feet and ankles with old scars extending to the knees of both legs. There was no evidence of venous insufficiency.

Biopsy of the skin revealed scleroderma and cutaneous calcinosis.

Roentgen examination of the chest disclosed extensive linear infiltration throughout the parenchyma of both lungs. Examination of the lower extremities showed extensive calcification of both the skin and muscle (Fig. 3, *A* and *B*). The roentgen impression was dermatomyositis.

Comment: This patient with scleroderma

demonstrated extreme soft tissue calcification of the type usually seen in dermatomyositis.

Case iv. T.S. This thirty-nine year old woman was admitted on April 2, 1958 complaining of arthritis of nine years' duration and chest pain of one and one-half years' duration. The arthritis was associated with swollen and painful joints of both hands, elbows, knees, and feet. The swelling and deformity were evident on examination.

Roentgen examination of the chest showed evidence of widespread infiltration of the pulmonary parenchyma. Examination of the hands and wrists revealed marked narrowing of all joint spaces and, in addition, there was evidence of destructive change in the lateral aspect of the head of the proximal phalanx of the third finger of the left hand (Fig. 4, *A* and *B*). Because of this destructive change, the roentgen impression was that of rheumatoid arthritis.

L. E. tests were positive on six different occasions.

Symptomatic relief was obtained with steroid therapy, but the disease followed a progressive course and the patient expired on March 3, 1959. Autopsy showed disseminated lupus erythematosus.

Comment: This patient with disseminated lupus erythematosus showed changes in the hands which closely resembled those of rheumatoid arthritis progressing to the stage of frank bone destruction.

Case v. C.M. This sixty year old woman was admitted on February 17, 1959 with complaints of generalized arthralgia and muscle weakness of sixteen months' duration. These symptoms had progressed until the patient had become bedridden. Two months prior to admission she noted dysphagia.

Physical examination showed marked muscular weakness, the muscles being flabby and atrophic.

Roentgen examination disclosed atony of the pharynx and esophagus with absence of peristalsis, suggesting scleroderma (Fig. 5, *A* and *B*).

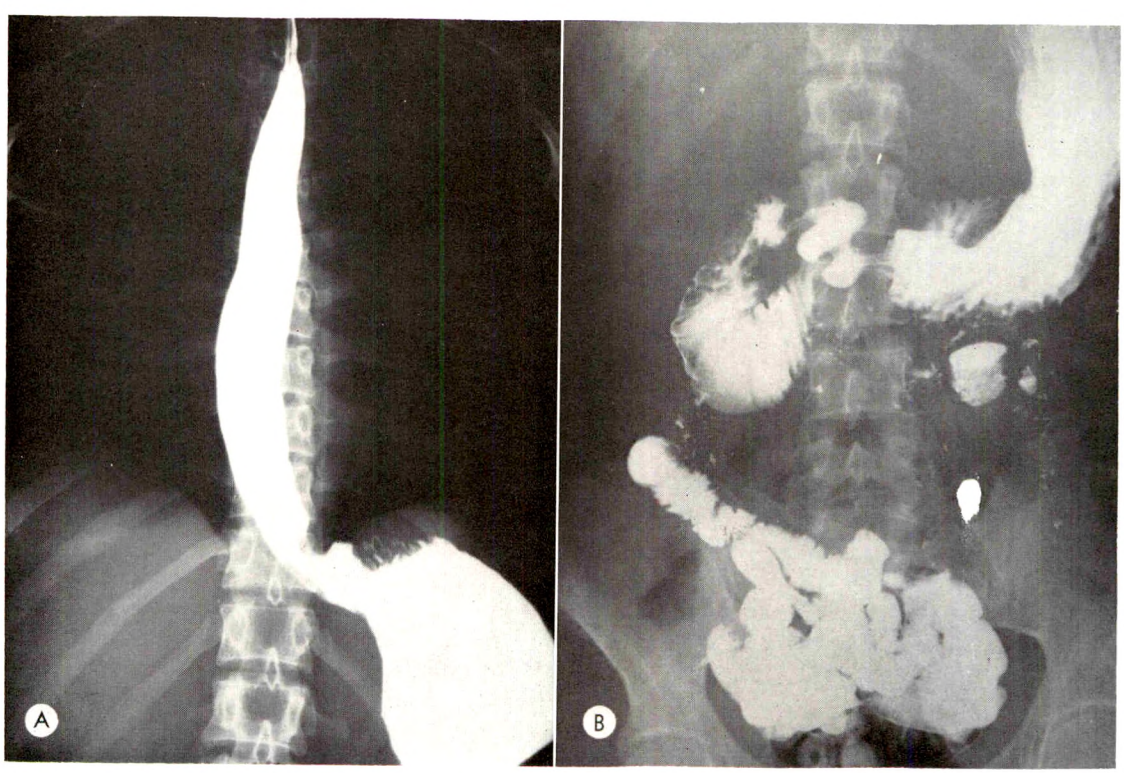


Fig. 2. Case ii. (*A*) Roentgenogram of the esophagus shows dilatation and atony. (*B*) Roentgenogram of the upper gastrointestinal tract shows dilatation of the duodenal loop.

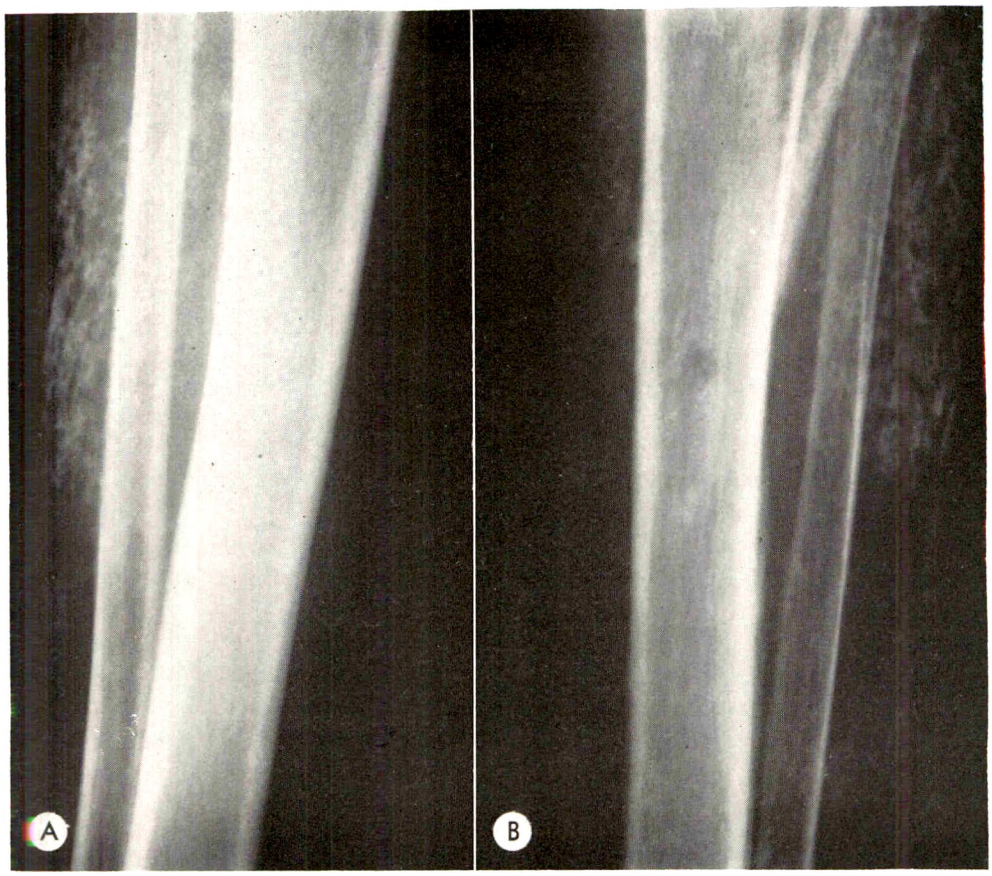


Fig. 3. Case III. (*A* and *B*) Roentgenograms of both lower extremities show extensive calcification of skin and muscle and irregularity of the soft tissues indicating areas of ulceration.

Electromyography was performed with a reading consistent with a myopathy. The muscle biopsy was reported as dermatomyositis.

Steroid therapy resulted in definite improvement of muscle strength, and relief of dysphagia. The patient did not return for follow-up visits, but a report from her family physician stated that she died in May, 1959 of an exsanguinating gastrointestinal hemorrhage.

Comment: This patient with dermatomyositis showed pharyngeal and esophageal changes considered typical of scleroderma.

DISCUSSION

Each of the patients reported here exhibited one or more roentgen findings which are considered more typical of a form of collagen disease other than the one which was actually present.

Cases I and II with unequivocal lupus erythematosus revealed roentgen findings in the gastrointestinal tract and soft tissues which are identical to those described in scleroderma,[4] and this diagnosis was therefore suggested. In scleroderma the esophagus is widened and atonic, with diminished peristalsis, and regurgitation from the stomach occurs. The small bowel is dilated, with diminished peristalsis. Delay in transit is observed. The heart may be enlarged. Also, in scleroderma soft tissue calcification occurs, most often in the hands, but it may be present elsewhere, particularly in areas subjected to pressure, as in the forearms of our Case I. The similarity of these changes to those seen in our Cases I and II is striking.

It is true that the gastrointestinal tract

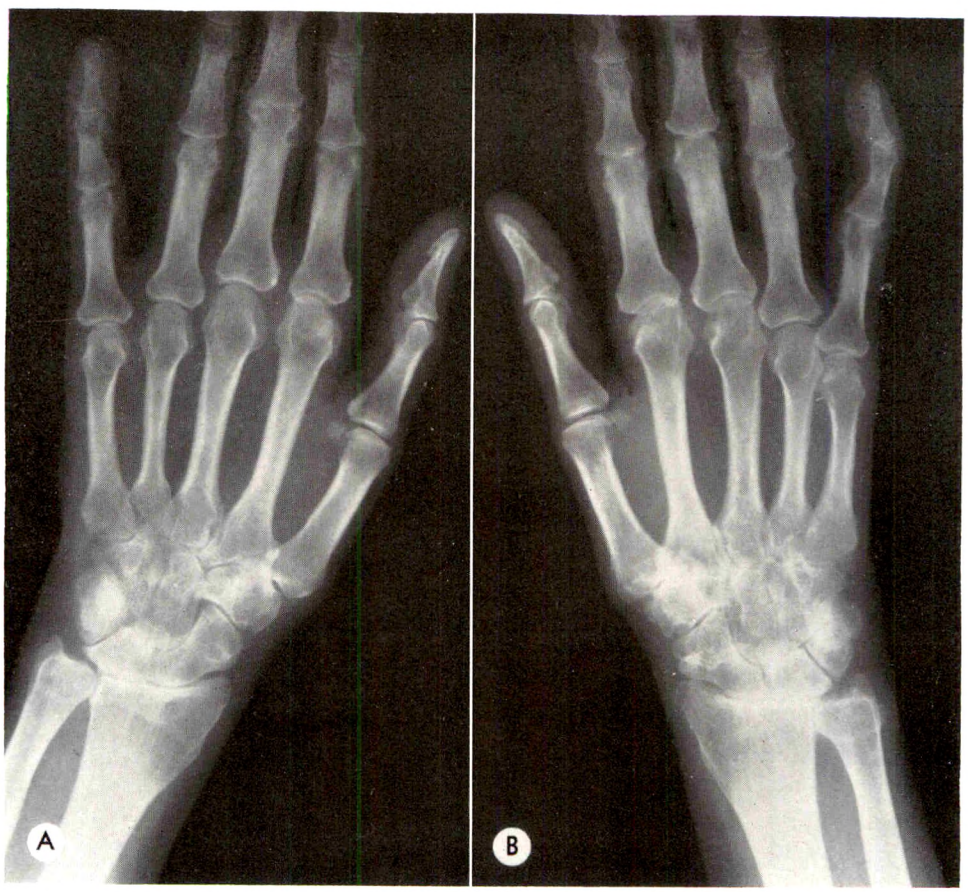


Fig. 4. Case iv. (*A* and *B*) Roentgenograms of both hands show osteoporosis, narrowing of joint spaces, and early destructive change in the proximal phalanx of the third finger of the left hand.

of patients with lupus erythematosus may show lack of tone, dilatation, and poor peristalsis, but usually these changes are much less severe than those seen in scleroderma and in our Case i.[3,6]

Case iii, a patient with proved scleroderma, demonstrated extensive cutaneous and muscular calcification, which is more usually related to dermatomyositis than to scleroderma.[7,9] The calcification in this patient was not discrete in periarticular or pressure areas, as commonly is seen in scleroderma.[4] For this reason it resembled more the amorphous cutaneous and muscular calcification of dermatomyositis, the diagnosis which was suggested roentgenologically.

Case iv, a patient with proved disseminated lupus erythematosus, showed evidence of an inflammatory arthritis with osteoporosis and narrowing of the joint spaces of the hands. These osseous findings may be seen in lupus erythematosus, but, unlike rheumatoid arthritis, they do not as a rule progress to the phase of bone destruction.[2,9] The evidence of destructive change in one finger suggested the diagnosis of rheumatoid arthritis. Combinations of rheumatoid arthritis and systemic lupus erythematosus do exist,[2] but in this patient there was no other evidence to suggest such an association.

Case v, a patient with proved dermatomyositis, showed severe alterations in pharyngeal and esophageal motility. Although an aperistaltic esophagus has been described in dermatomyositis,[6] it is seen most consistently in scleroderma and usually suggests the latter diagnosis.

The data presented here are further evi-

dence for the concept that all of these diseases are systemic alterations of the connective tissue and that their pathogenesis may be similar. Since connective tissues can respond to injury in only a limited number of ways, it is not surprising that the clinical and roentgen manifestations of diseases of connective tissues may closely simulate each other and may, in fact, be indistinguishable.

These cases also illustrate the fallibility of over-reliance on any single roentgen change and the lack of specificity of these changes. A correct diagnosis requires the combined information derived from clinical, roentgen, and laboratory sources.

SUMMARY

Five cases of collagen disease (3 of systemic lupus erythematosus, 1 of scleroderma, and 1 of dermatomyositis) are reported. Each of these cases presented extrapulmonary roentgen findings which are, as a rule, more typically seen in some other form of this family of diseases. Clinically and roentgenologically, these diseases are poorly defined and undue reliance should not be placed on a single roentgen manifestation.

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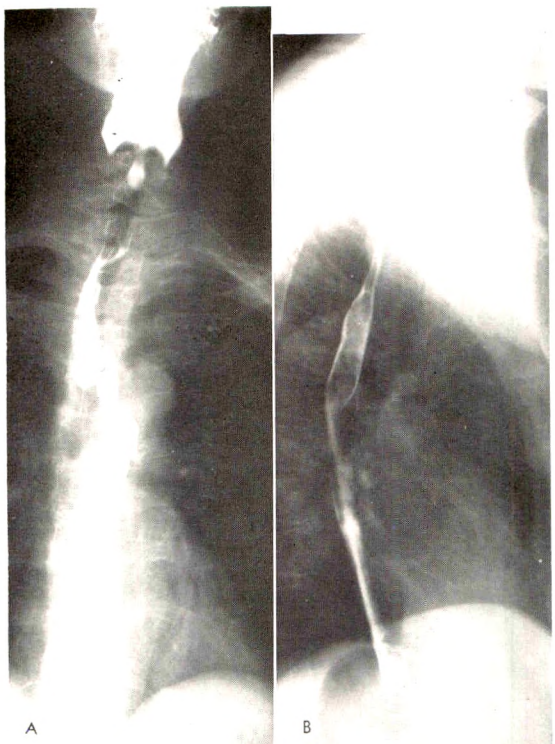


FIG. 5. Case v. (*A* and *B*) Roentgenograms of the esophagus show stasis of barium in the pharynx and esophagus and absence of peristalsis.

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THE ROENTGEN APPEARANCE OF MUTILATING PALMO-PLANTAR KERATOSIS*

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THE disease characterized by the formation of disabling hyperkeratoses of the skin of the palms and soles is best known as palmo-plantar keratosis or keratoma, but it is also called by the following synonyms: keratoderma, hyperkeratosis palmaris et plantaris,[1,2] tylosis palmarum et plantarum, ichthyosis palmaris et plantaris, symmetric keratodermia of the extremities,[4] and Méléda disease.[3] The multitude of synonyms is due in part to the difference in degree and extent of the disease process and to the other ectodermal dysplasias which may be associated with it.[7] The mutilating form of this disease is rare, however, and to our knowledge the case reported herein is the most extensive yet described. The mutilations of palmo-plantar keratosis offer characteristic roentgenographic changes from which the diagnosis can be made or strongly suspected.

HISTORICAL REVIEW

In 1826 Stulli described an endemic, congenital disease occurring in the inhabitants of the island of Méléda in southern Dalmatia which was manifested by hyperkeratosis involving chiefly the palms and soles.[4,8] Stulli's cases were initially thought to be endemic leprosy, but were later identified as the same palmar and plantar keratoma described by Thost in 1880 and Unna in 1883.[8] The hereditary and familial nature of the disease probably explains the high incidence on Méléda, where intermarriage occurred frequently in an isolated community.[4]

ETIOLOGY AND CLINICAL COURSE

Palmo-plantar keratosis is characterized by symmetric thickening of the horny layer of skin beginning on the palms and soles and occasionally extending over the dorsal surfaces, especially about the metacarpophalangeal joints.[4,6] It may be congenital or acquired. The acquired form, an uncommon variant, appears to be secondary to eczema, infection, psoriasis or toxic dermatoses (arsenic).[3] In the congenital form heredity is the important factor. Many authors have cited multiple cases occurring through several generations of a given family.[4] Turpin *et al.*,[7] for example, followed the development of the disease through six generations in 15 members of a family of 28 individuals. He suggested that the genetic character is monogenic, autosomal and dominant.

Congenital palmo-plantar keratosis is rarely manifest at birth and is generally not recognizable until the third or fourth month of life. Occasionally it may not appear before four or five years of age, even when of congenital origin. The hyperkeratosis begins as patches of epithelial thickening which grow and coalesce until they form thick, smooth, yellowish-white, translucent, hard plates over the palms and soles. The palms are eventually completely covered by these plates, while, as a rule, only the weight-bearing portions of the soles are involved. The horny plate becomes rigid and inelastic, predisposing to the formation of fissures.[3,4] Further, in both the congenital and acquired forms of keratoma, hyperhidrosis soon develops, resulting in maceration and additional fissuring of the lesions.[3–5,7–9] With maceration comes infection, and the hyperkeratoses lose their plate-like appearance and assume a dirty gray to brown color and a verrucous surface, and they may become odoriferous. Hyperkera-

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toxic lesions may later appear on the dorsa of the hands, and on the knees, elbows, in the groin, or on any other area of the skin at which pressure due to weight bearing or clothing abrasion may occur.[8]

In certain severe cases, mutilation in the form of spontaneous amputation of digits may occur.[8,9] This seems due in part to the development of deep, annular, horny, constrictive bands which form about the digits and which seem to be peculiar to the mutilating form of palmo-plantar keratosis. Additional mutilation may occur as the result of fissuring, infection and consequent trophic complications due to scarring and pressure upon nerves and vessels.

The histopathology is nonspecific. The skin layers are uniformly thickened with excessive cornification and may be otherwise normal.[4] The lesion may be confused pathologically with psoriasis. When fissures have developed, infflammatory changes are present because of secondary infection.

In the usual form of palmo-plantar keratosis, roentgenographic findings do not ordinarily contribute to the diagnosis, but, when the mutilating form is present, roentgen manifestations characteristic of this entity will appear and they are described below.

REPORT OF A CASE

R.R., a Negro male, was born September 20, 1941, the third of four children. Although apparently normal at birth, at two months of age he developed a persistent, rough, erythematous, scaly rash over the inguinal area and buttocks. At eighteen months, patches of dry, scaly, thickened skin appeared on the soles and similar lesions on the palms three months later. These hyperkeratoses rapidly spread to involve the entire palmar, and much of the plantar, surfaces. The disease process continued and, at the age of five years, the skin over the palms, soles, inguinal and perineal regions was scaly and thickened with layers of dead skin. The extremely thick keratoses of the palms and soles caused swelling and spreading of the digits. At that time, the left hand showed amputation of the distal phalanx of the fourth finger and a wet granulating stump of the distal phalanx of the fifth finger. In addition, the skin over the knees and elbows showed keratotic plaques. There was kyperkeratotic skin about the corners of the mouth, the ears, the penis and scrotum.

Roentgenograms of the extremities made at the age of five are said to have shown demineralization of the metacarpals and phalanges with resorption of the tufts of all the distal phalanges. There were destructive lesions involving several of the other phalanges, and, of course, the amputations were apparent.

At the age of eight the distribution of the lesions was the same but the hyperkeratoses had become larger, forming dense, fissured, woody masses which extended deep into the palms. The hands were claw-like and functionless. The fingers and thumbs showed progressive atrophy with proliferation of keratin tissue about the nails, and on the basis of this latter change an erroneous diagnosis of pachyonychia congenita was made. The distal portions of the fingers were atrophic and about the size of an infant's digits. The feet showed the same findings as the hands with slightly less atrophy of the digits. Several more distal phalanges of hands and feet were absent.

Pathologic examination of a biopsy specimen from the sole of the left foot showed marked hyperkeratosis with piling up of excessive keratohyalin material on the epithelial surface. Epithelial hyperplasia was seen with widening of the stratum granulosum and elongation of the rete pegs. Diffuse chronic inflammatory infiltration was present.

When he was eight years old the patient had prolonged hospitalization for surgical procedures on the feet which included amputation of the remaining toes and resection of the plantar surfaces. Pedicle grafts were brought to the under surfaces of the feet from the thighs. Due to infection, the right foot had to be grafted twice. Then, as happened so many times throughout his course, the patient was lost to follow-up for a lengthy period.

At the age of fourteen the patient was admitted to the hospital twice for staphylococcal septicemia arising from the infected extremities. At that time the skin grafts on the plantar surfaces were intact, and, of course, the toes had been previously amputated. All fingers were now missing from the hands as a result of autoamputation, and, due to the development of hyperhidrosis, macerated, fissured skin covered palmar and dorsal surfaces.

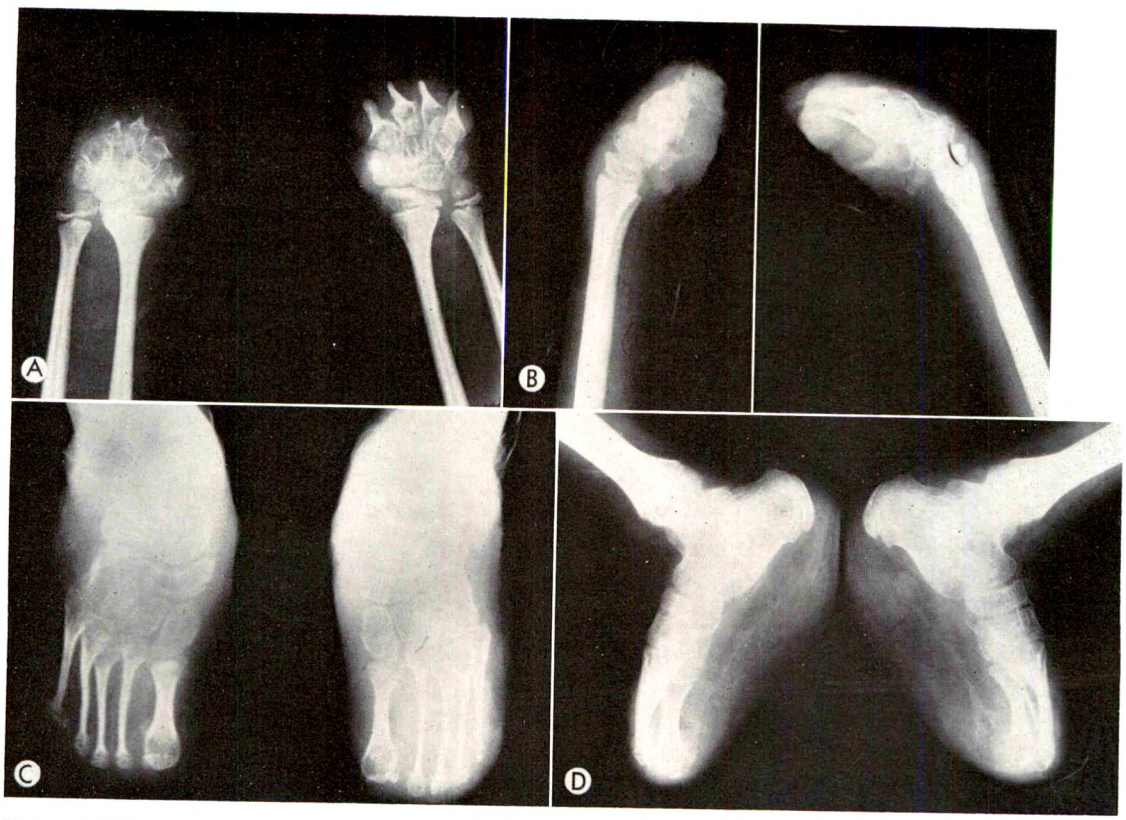


FIG. 1. (*A*) Posteroanterior roentgenograms of the wrists and hands, made at the age of fourteen, show preservation of mineralization of bones, but there is amputation of bones and soft tissues at the level of the metacarpal bases. There is some thinning of the distal shafts of the radii and ulnae. The remaining soft tissue of the hands appears somewhat irregular. (*B*) Lateral roentgenograms of the hands and wrists show thick, featureless soft tissue over the palms. Surgical dressings are in place. (*C*) Anteroposterior roentgenograms of the feet, made at the age of fourteen, show amputations of all toes at the level of the metatarsal heads. Mineralization is, in general, good, although there is trophic thinning of the shafts of all metatarsal bones. (*D*) Lateral roentgenograms of both feet show thickening of the soles due to replacement of the keratomatous plantar tissue by fatty skin grafts. All prints were made from microfilm reproductions.

Roentgenograms of the extremities made at the age of fourteen (Fig. 1, *A–D*) show slight demineralization of bone. Autoamputation, probably a result of cornified bands, the pressure exerted by abnormal tissue masses, and inflammatory scarring, has extended to the level of the metacarpal bases in the hands (Fig. 1, *A* and *B*) and to the metatarsal heads in the feet (Fig. 1, *C* and *D*). Figure 1*D* shows the thick, fatty skin grafts applied over the soles of the feet six years earlier.

The patient returned recently, now nineteen years old, and was seen by us for the first time. There was abundant evidence that the destructive process had continued. The hands and feet were now macerated stumps partially covered with warty, nodular keratotic plaques (Fig. 2, *A* and *B*). The skin graft on the left foot was largely replaced by verrucous, macerated keratoma tissue, but the right skin graft was intact with keratomatous change about its margins (Fig. 2, *C* and *D*). Hyperkeratotic plaques were present on the skin about the knees (Fig. 2*C*), elbows and sacrum. There was hyperkeratosis to a lesser degree under the arms, about the groin and about the ears. Review of these findings, and of pertinent dermatologic literature, led us to the diagnosis of mutilating palmo-plantar keratosis.

Roentgenograms made at the present time (Fig. 3, *A*, *B* and *C*) show that there has been progressive loss of bone during the past five years (compare with Figure 1, *A–D*). All metacarpals have now been lost from the hands (Fig. 3*C*) and there is fusion of the remaining carpal elements, possibly the end result of

superimposed bone infection. Note that mineralization is rather well preserved. There is thinning of the distal aspects of the shafts of the left radius and ulna, and periosteal reaction, perhaps the product of infection, is seen along the distal medial ulnar shaft. Especially noteworthy is the appearance of the soft tissues on the roentgenogram, for one can see the nodular, warty appearance characteristic of infected, macerated keratoma tissue. These findings are ever more striking on the roentgenograms of the left foot. There has been further autoamputation of all of the metatarsals and some of the tarsal bones in the left foot (Fig. 3*A*) and of the distal second, third and fourth metatarsals in the right foot (Fig. 3*B*). Note the trophic thinning of the shafts of the first and fifth right metatarsals (Fig. 3*B*).

The patient himself is mentally alert and intelligent, and he can use his upper extremity stumps to feed himself and to write. Future management will include removal of the stumps,

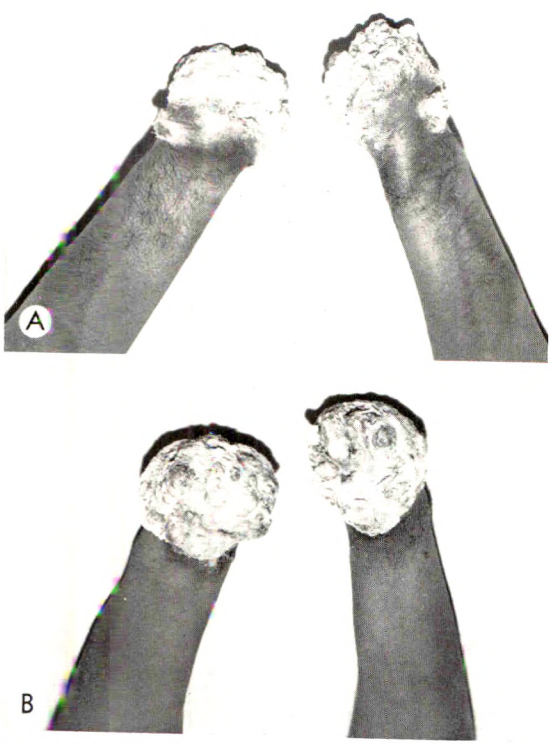


FIG. 2. (*A*) Photograph of the dorsal surfaces of the arms, made at the age of nineteen. Note destruction of the hands and replacement by nodular, fissured, macerated tissue. (*B*) Volar surfaces of the wrists and hands showing warty, macerated keratomatous tissue.

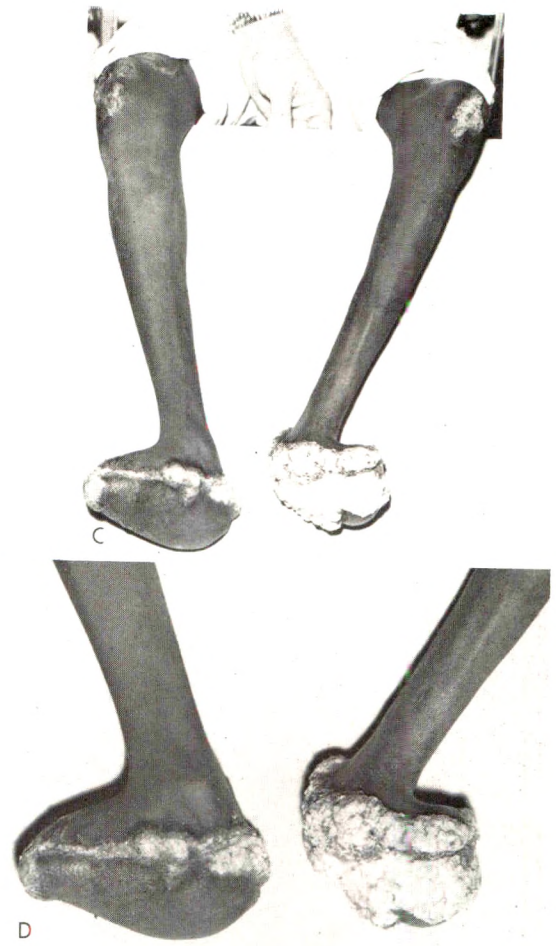


FIG. 2. (*C*) Photograph of the legs and feet, made at the age of nineteen, shows replacement of the left plantar graft by keratomatous tissue which has appeared along the margins of the still-preserved graft on the sole of the right foot. Note hyperkeratotic lesions over the knees. (*D*) Close-up of the feet.

which are unsightly and a source of infection, and the development of prosthetic devices which will fit in such a way as to exert minimum pressure on the skin and so avoid the development of new areas of kyperkeratosis. Thorough questioning of the patient's family yields no history of skin lesions of any sort.

DISCUSSION

Palmo-plantar keratosis is an ectodermal defect, commonly, perhaps always, congenital in origin, manifested by a tendency toward excessive cornification of the skin of the palms and soles as well as at other pres-

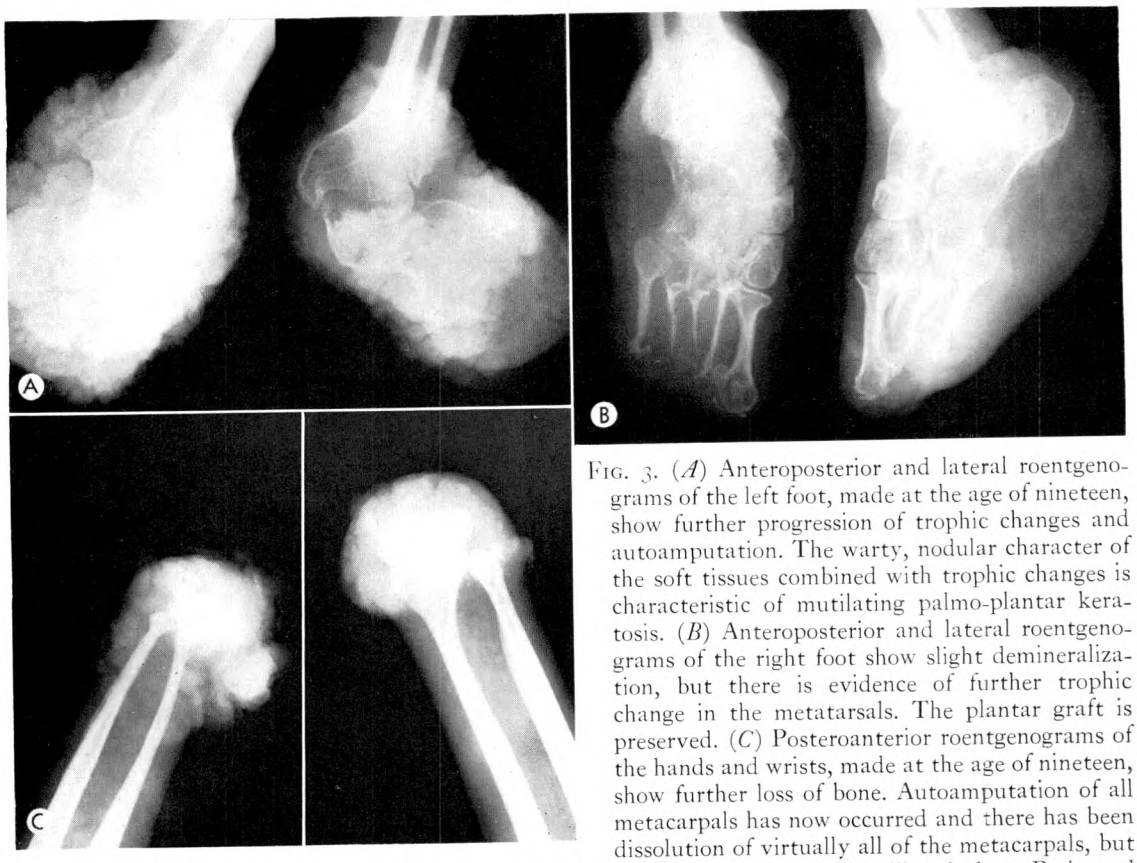


FIG. 3. (*A*) Anteroposterior and lateral roentgenograms of the left foot, made at the age of nineteen, show further progression of trophic changes and autoamputation. The warty, nodular character of the soft tissues combined with trophic changes is characteristic of mutilating palmo-plantar keratosis. (*B*) Anteroposterior and lateral roentgenograms of the right foot show slight demineralization, but there is evidence of further trophic change in the metatarsals. The plantar graft is preserved. (*C*) Posteroanterior roentgenograms of the hands and wrists, made at the age of nineteen, show further loss of bone. Autoamputation of all metacarpals has now occurred and there has been dissolution of virtually all of the metacarpals, but good mineralization is maintained. Note beginning trophic changes in the distal radii and ulnae. Periosteal reaction along the medial aspect of the distal left ulna may be the result of osteomyelitis from the always-prevalent soft tissue infections. Soft tissues show the characteristic irregular, lumpy appearance of far-advanced palmo-plantar keratosis.

sure points about the body. The most morbid form of this disease, apparently a rare complication, will progress to mutilation in the form of autoamputation of phalanges and soft tissues of the digits, later extending to metacarpal and metatarsal regions. Autoamputation of digits may be caused by circumferential cornified bands with embarrassment of blood supply and innervation, but the destructive changes in the palms and soles, and probably to some extent in the digits as well, seem also to be the result of pressure on bone, nerves and vessels by keratomatous masses, and possibly of inflammatory scarring produced by repeated infections that occur in the deep clefts of the macerated, verrucous keratoma tissue. In the case reported above, yet another type of bone change was present. It is illustrated by the fusion of carpal elements seen in Figure 3*C* and is probably the end result of healed osteomyelitis and infectious arthritis transmitted from infections constantly present in the abnormal overlying soft tissue.

There is a lengthy list of disease entities which can cause terminal phalanx or digit resorption, including collagen diseases such as scleroderma and rheumatoid arthritis, and such processes as Raynaud's disease, thromboangiitis obliterans, syringomyelia, frostbite syndrome and ergot poisoning. Seldom does bone atrophy in these conditions extend to proximal phalanges or beyond. Digital autoamputation can occur in the fifth, and occasionally the fourth, toe in ainhum, but probably the disease most seriously to be considered in the differential

diagnosis of the findings described in our case above is leprosy. In the neural form of leprosy progressive distal atrophy and autoamputation can occur, as can soft tissue ulceration and secondary osteomyelitis. A useful objective roentgen differential diagnostic point is the identification of the nodular, warty keratoma tissue, well illustrated in Figure 3, *A* and *C*, which is the product of fissuring of the macerated horny plates produced by the dystrophic epithelium in palmo-plantar keratosis.

As a matter of interest, it can be said that treatment of palmo-plantar keratosis remains supportive, with the application of softening unguents to prevent cracking of the horny epithelial plates present initially, the administration of antibiotics for deep infections which may occur, and surgical relief of digital compression bands. In the case we have described this treatment could not be carried out, but whether it would have been of avail in preventing the mutilation which has occurred is not known.

SUMMARY AND CONCLUSIONS

1. A congenital familial disease, palmo-plantar keratosis, is initially manifested by dense thickening of the epithelium of palms and soles, and of the skin at pressure points about the body. Later, maceration may occur as the result of hyperhidrosis.

2. A morbid variant of this disease may produce mutilation in the form of autoamputations of digits, and finally of the entirety of the hands and feet.

3. The findings of trophic bone atrophy combined with regularly nodular, verrucous soft tissue are thought to afford a relatively absolute basis for roentgenologic identification of this entity.

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SOME ROENTGEN FEATURES OF PAGET'S DISEASE*

By HOWARD L. STEINBACH, M.D.
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PAGET'S disease, an entity of unknown etiology, is found in over 3.5 per cent of the population beyond the age of forty-five years.[5,19,20] The incidence increases until the age of seventy-five after which it levels off. The disease affects males more often than females[20] and shows a familial predisposition.[10,17] Most cases are detected initially as incidental findings on roentgenograms obtained for other purposes. Other patients may see a physician because of pain, fracture, deformity of an extremity, increased head size, or warmth of the overlying skin. Some cases are discovered by dentists when they find hypercementosis or ankylosis of a tooth, or deformity of the jaws. Deafness from involvement of the inner ear or signs of malignant degeneration of an involved bone may be the first indications of the disease.

The disease is localized to one or more bones, although, rarely, all, or almost all, of the bones may be affected.[1] According to Dickson *et al.*,[7] the pelvis is the most common site of the disease, with involvement of the femur, spine, skull, and tibia next in frequency, respectively (Table 1).

TABLE 1

LOCATION OF OSTEITIS DEFORMANS IN 367 CASES*

Site of Involvement	Cases†	Combined Phase‡ (100 cases)	Sclerotic Phase‡ (100 cases)
Pelvis	243		
Iliac bones	—	107	100
Ischia	—	97	73
Pubic bones	—	96	73
Femur	171	68	40
Skull	153	—	—
Tibia	127	51	22
Sacrum	—	42	35
Lumbar spine	103	38	30
Dorsal spine	51	16	9
Clavicle	33	8	15
Humerus	20	9	1
Ribs	12	2	—
Scapula	7	1	—
Radius	7	1	—
Cervical spine	6	2	—
Fibula	6	2	—
Ulna	5	1	—
Os calcis	4	1	2
Patella	4	2	—
Talus	1	—	1

* Reprinted with permission of *Radiology*.[7]
Not including bones of the face and base of skull. More than one site of involvement in a number of cases.
† Cases of involvement of given site among total 367 cases.
‡ Classified roentgenographically. In these columns bilateral involvement is counted twice.

PATHOLOGY

Macroscopically, in advanced cases, the involved bone is thickened and presents a rough, uneven surface. Long bones are frequently deformed; compact bone is replaced by lamellated spongy bone of varying density, and the marrow cavity is wide or narrow. In cranial involvement, the bones of the vault of the skull are sometimes greatly thickened. The inner and outer plates and diploë may not be distinguishable, with the entire thickness consisting of spongiosa. If the base of the skull is involved, it sometimes bulges into the cranial cavity. The bones and periosteum are frequently vascular and the vessels leading to the bones are enlarged.[8,15]

Paget's disease is primarily one of bone destruction. Osteoclastic resorption of the trabeculae of the spongiosa or the walls of the haversian canals of the compacta is followed by connective tissue proliferation. Immature membranous bone is formed, which is destroyed and reconstituted repeatedly, producing the irregular, numerous cement lines and characteristic mosaic pattern described by Schmorl.[20]

* From the Department of Radiology, University of California, School of Medicine, San Francisco, California. This work was supported in part by Research Grant A-2589 GM, National Institutes of Health, U. S. Public Health Service.

Extensive involvement stimulates the periosteum to produce bone which is resorbed and converted to Paget's bone, resulting in expansion of the cortex.

The destructive process is self-limited and almost invariably is followed by osteogenesis, which is a manifestation of healing. Osteogenesis is stimulated by stress, such as weight bearing, and is inhibited by immobilization to a greater extent in Paget's disease than in normal bone.

The serum alkaline phosphatase, which represents the degree of osteoblastic activity, is elevated in cases with extensive involvement and active disease. It is least elevated in the healed or sclerotic phase. The sedimentation rate is also frequently elevated with active Paget's disease.[11]

PATHOLOGIC FEATURES OBSERVED ROENTGENOGRAPHICALLY

Many of the pathologic features of the disease can be observed roentgenographically, particularly if serial roentgenograms made over a period of years are available. One such process, that resulting in the deformity of bones present in advanced cases, can be observed readily in the sequence of events leading to lateral curvature of the femur or anterior curvature of the tibia. Weight bearing produces tension forces upon the lateral surface of the femur and compression forces on the medial surface.[9] The extremely active and weakened Paget's bone responds with periosteal apposition on the surface subjected to tensile forces, leading to a lateral expansion of the bone. This process may be followed by resorption of the opposite cortical surface proceeding at an almost equal rate and by compensating apposition and resorption of the endosteum, which maintains the medullary canal (Fig. 1). The curvature of the tibia is the result of bone apposition on the anterior surface followed by resorption of the posterior surface (Fig. 2 and 3). Here too, apposition is on the side of the bone subjected to tension, and resorption on the side where compression exists. This explanation also accounts for elongation of the bone. It is readily apparent in the curved tibia that the bone is longer than normal, as, despite the curvature, the upper and lower ends maintain their relationship with the normal fibula. A similar mechanism is assumed to be responsible for the curvature of other long bones (Fig. 4), the basilar invagination of the skull, and inward protrusion of the acetabula and adjacent structures in the pelvis (Fig. 5). The forces responsible may be due to muscle pull or gravity.



FIG. 1. Increased convexity of the left femur from bone apposition along the lateral surface. Slight resorption of medial subcortical surface has produced curvature. Bone deposited upon the medial endosteal surface, without corresponding resorption of the lateral endosteal surface, results in a narrow medullary canal.

The process of apposition and attrition of bone is frequently seen in migrating teeth and in the enlarged sella turcica caused by a pituitary tumor. It operates normally in the enlargement of the calvarium with growth of the brain.

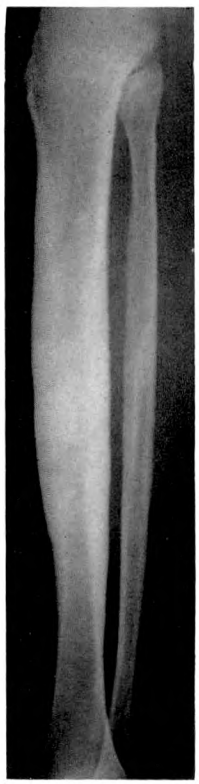


Fig. 2. Bone apposition on the right tibia anteriorly without resorption of the posterior surface.

Table II

INCIDENCE OF PATHOLOGIC FRACTURE IN 367 CASES OF OSTEITIS DEFORMANS*

Location of Fracture	Patients
Thoracic portion of spinal column	24
Lumbar portion of spinal column	24
Right femur	8
Left femur	1
Right tibia	6
Left tibia	3
Right humerus	1
Left humerus	1
Separation of tibial tubercle	2
Ischium (only ununited fracture observed)	1
Basioccipital protrusion (extensive)†	6
Total number of pathologic fractures among 62 patients	77

* Reprinted with permission of *Radiology*.[7]

† The present author does not consider basioccipital protrusion to represent a fracture.

FRACTURES

The bones in Paget's disease, although sometimes appearing strong, are much more prone to fracture than normal bone when subjected to a bending force, particularly during the destructive phase.[2,9,11] The fractures may be complete, are usually transverse, or occasionally oblique, and most frequently occur in the spine or upper part of the femur and tibia (Table II). Collins[5] found 9 fractures in 70 patients, but only 1 in a routine survey of 650 consecutive patients, 24 of whom had Paget's disease. He estimated that the incidence must be less than that indicated in published reports and not more than 1 per cent of all cases.[5] The fractures heal readily, the



Fig. 3. Marked anterior bending deformity of the left tibia due to bone apposition anteriorly and resorption posteriorly. An almost equal apposition on the posterior endosteal surface and resorption of the anterior endosteal surface maintains the width of the medullary canal. Although curved, the ends of the tibia maintain an almost normal relationship with the fibula, indicating increased bone length.

callus converting to the same type of mosaic structure as the surrounding bone.

The fractures in the femur and tibia are more often incomplete, extending from the periosteum to the medulla in the shaft or for varying distances into the cancellous bone at the ends. These fractures occur along the lateral surface of the femur or the anterior surface of the tibia. They appear on roentgenograms as fissures lying perpendicularly to the long axis of the bone (Fig. 6*A*). Occasionally, if they have been present for several days or weeks, the margins of the defects are sclerotic. The incomplete fractures have been confused with the pseudofractures of osteomalacia but can usually be differentiated by their position (Fig. 17). Pseudofractures in osteomalacia involve the medial surface of the shaft or



FIG. 4. Bending and elongation of the radius due to periosteal and endosteal apposition and resorption; also slight bone growth distally as the articular surface and styloid process of the radius extend beyond the usual relationship with the ulna.

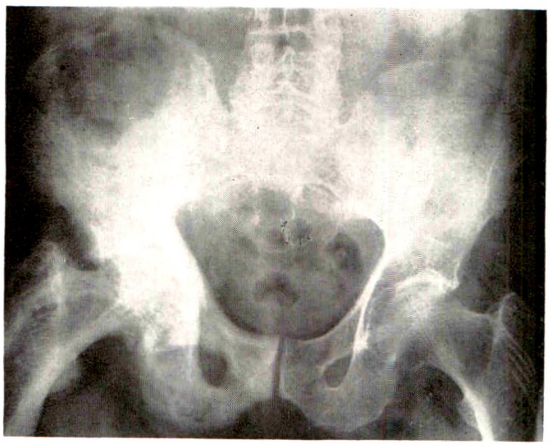


FIG. 5. Bending inward of the medial wall of the right side of the pelvis due, primarily, to bone apposition. Some resorption of the acetabular surface, indicated by migration of the femoral head medially. The uniformly narrow articular cartilage of the right hip is presumably due to the resumption of endochondral ossification without corresponding cartilage proliferation. The early, primarily destructive stage of Paget's disease is demonstrated in the upper end of the left femur and in the left innominate bone. There are thickened bone bundles along the lines of stress.

superior surface of the neck of the femur; they are associated with generalized bone disease and frequently are almost symmetric bilaterally.[14,25]

Two factors are probably responsible for the location of the incomplete fractures: (1) When a sudden or heavy load is exerted upon the lower extremity, the tension or stretch exerted along the lateral aspect of the femur and the anterior surface of the tibia breaks the structurally weak Paget's bone. The forces along the opposite surfaces of these bones are those of compression and, therefore, do not produce fractures. (2) The fractures tend to occur in the region of bone resorption at the advancing margin of the lesion. The disease usually begins at the upper end of the femur or tibia and it is here, where the tensile forces are greatest, that the highest incidence of fractures is found. Occasionally the disease originates at the lower end, or at both ends simultaneously, and, regardless of the site of origin, as the disease spreads, additional fissure fractures occur at intervals, some-

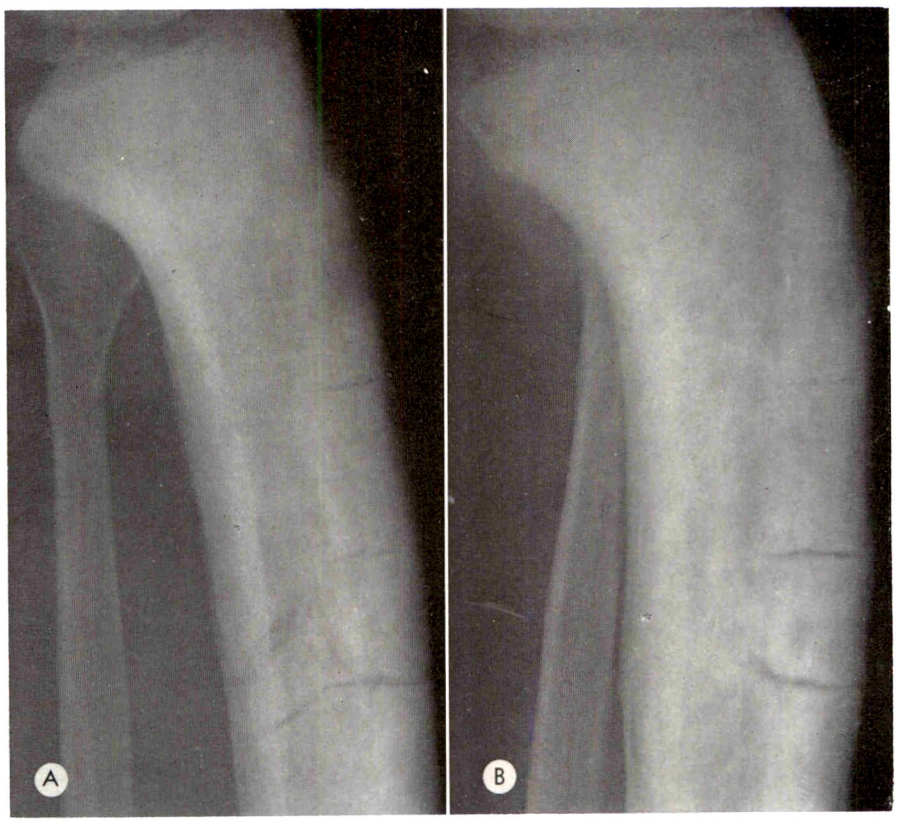


FIG. 6. (*A*) Lateral roentgenogram of the tibia obtained after the patient experienced sudden pain. The lower 2 of 4 horizontal lines visible are horizontal fractures of the anterior cortex, but they extend obliquely downward and posteriorly to involve the posterior cortex. Soft tissue swelling was visible adjacent to the fractures. The upper two lines, covered by bone along their endosteal and periosteal surfaces, represent residual defects from old fractures. (*B*) Roentgenogram several months later. Prompt healing of posterior extensions of the fractures, probably because the fragments were approximated by compressive forces. The persistent anterior defects have joined the upper two defects as permanent scars.

times almost equidistant from each other (Fig. 7).

The fresh cortical fractures are associated with pain. When the anterior surface of the tibia is involved, a localized soft tissue swelling is visible on lateral roentgenograms. Shortly after the fracture is sustained, the periosteum forms bone over the fracture and for a variable distance surrounding it, leading to further thickening of the cortex. Endosteal bone also forms, limited to the immediate vicinity of the fracture and encroaching upon the medullary canal. Thus, the ends of the fractures are covered but the bony defect in the center of the cortex remains as a permanent scar. In some cases, a series of such scars attest to numerous previous traumata. The scars can be differentiated from recent fractures because they do not extend out to the periosteal surface of the cortex (Fig. 6, *A* and *B;* and 7). Although fissure fractures with complete healing were reported in the earlier literature, this was not true in our experience, possibly because our patients usually were treated on an ambulatory basis or with limited immobilization to avoid such complications as increased destruction of bone, hypercalcemia, and renal calculi. Perhaps continued weight bearing may prevent complete healing and lead to fibrous union. Where fractures extended completely across the shaft of a bone, the surface subjected to compression forces healed early, whereas defects persisted on the opposite surface (Fig. 6*B*).

CYST-LIKE DEFECTS

Radiolucent cyst-like defects of various size, surrounded by dense bone, may be seen in the spongy bone of the pelvis, the head and neck of the femur and other bones, and in deep layers of compact bone. These are collections of fat, resulting from necrosis and liquefaction of the proliferating fibrous tissue.[12]

CLASSIFICATION

The roentgen appearance may be classified into three descriptive forms: (1) sclerotic, (2) mixed, and (3) radiolucent. Multiple bone involvement may show similar or dissimilar lesions. Sometimes a single bone may exhibit more than one type of lesion.

Sclerotic Form. When present in cancellous bone, this consists of a uniform thickening of the trabeculae with a consequent

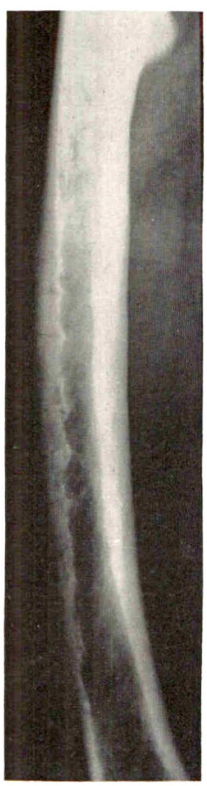


FIG. 7. A series of cortical defects along the lateral surface of the femur, representing healed fractures. Bone covers their periosteal and endosteal surfaces. Characteristically, the periosteal new bone is smooth surfaced, whereas the endosteal surface is irregular because of bone repair limited to the immediate region of the fracture.

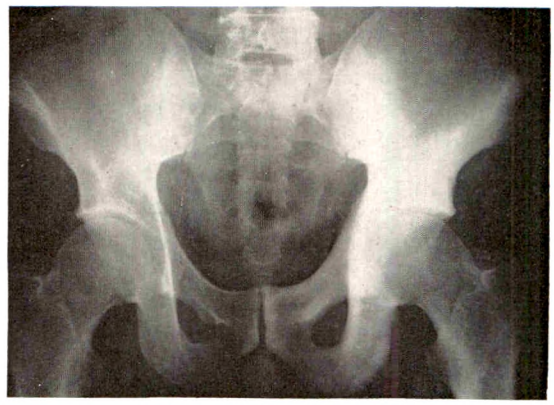


FIG. 8. Sclerotic Paget's disease of the left innominate bone.

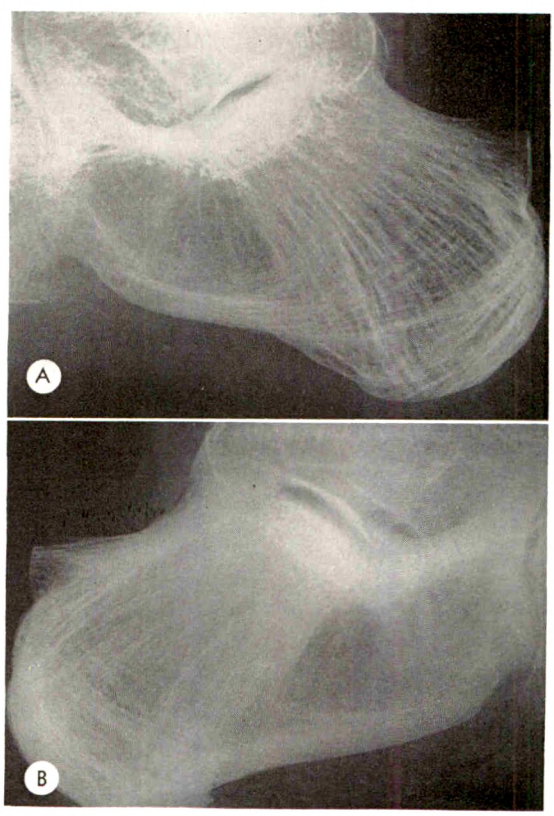


FIG. 9. Lateral roentgenograms of the right and left calcanei from the same patient. (*A*) Early active stage. Thick bundles organized along lines of stress and crossing at approximately right angles superimpose upon the generalized radiolucent bone. (*B*) The disease approaches the healed or quiescent stage.

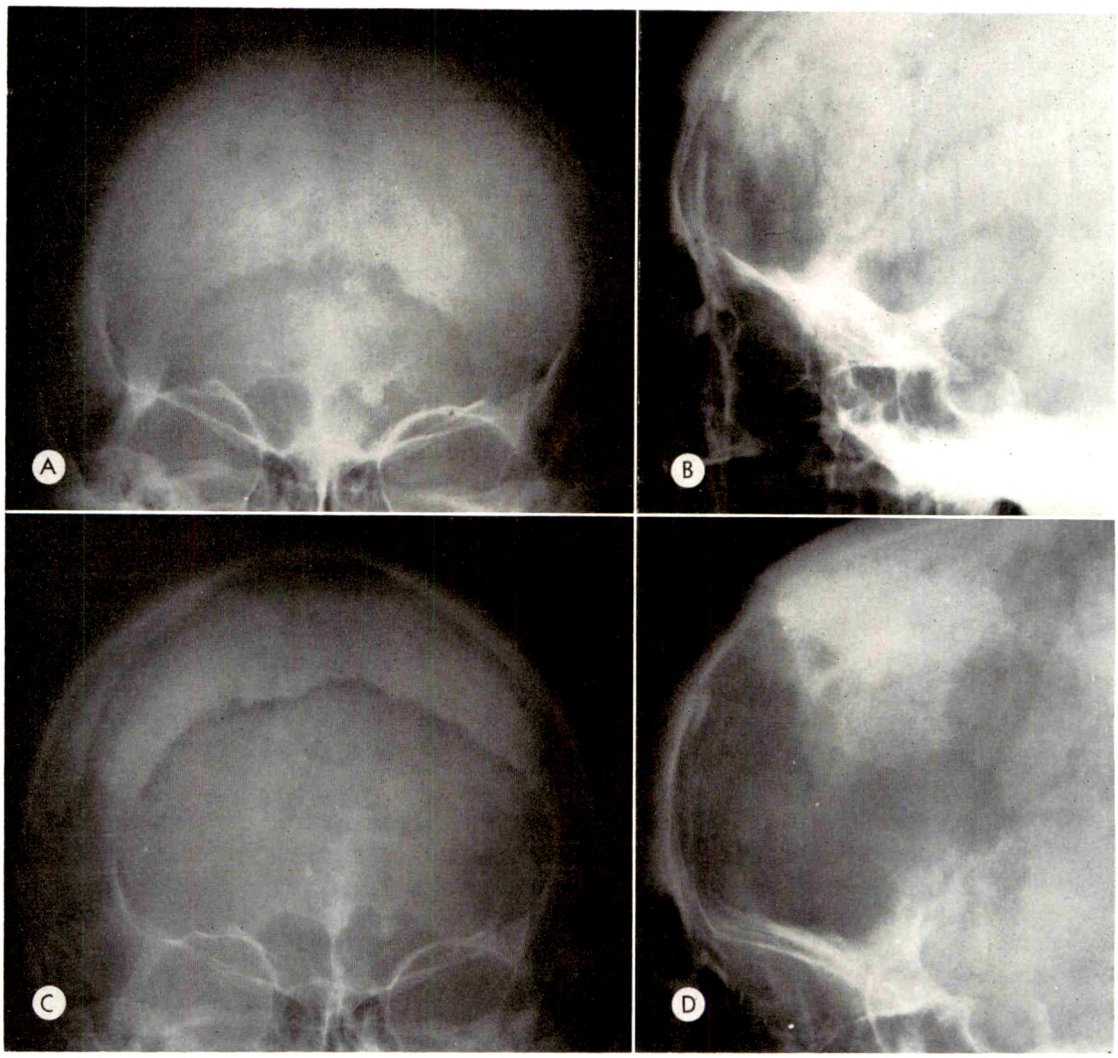


FIG. 10. (*A* and *B*) Osteoporosis circumscripta of the frontal bone. (*C* and *D*) Approximately five years later. The advancing margin is sharply demarcated from the normal bone. The meningeal vascular grooves are not obliterated as the meningeal surface of the inner table has not been destroyed.

decrease in the size of the marrow spaces; the surrounding cortex is thick and the bone is increased in size (Fig. 8). Sclerosis is seen frequently in the pelvis, vertebrae, clavicles, facial bones, ends of the long bones, base of the skull, and bones of the wrists, hands, and feet. The ribs, not commonly involved, also may be sclerotic.

In the long bones, the cortex is thickened and dense. The medullary cavity may be widened or narrowed, and in some cases almost obliterated (Fig. 1). The cancellous portions at the bone ends frequently have longitudinally thickened trabeculae. In some cases, sclerosis of the cortex is associated with the mixed type of involvement of the cancellous ends.

The sclerotic form represents the healed or end stages of the disease. The bones appear massive and strong, but because of the structurally inferior composition are more fragile than normal bones. Complete and fissure fractures occur but are less common than in the other more active forms of the disease. Of 27 fissure fractures reported by Dickson *et al.*,[7] 23 were in the combined form and only 4 in the sclerotic form of the disease.

Mixed Form. This form is the most common and may be present in any part of the skeleton. The homogeneous cortex is replaced by a cancellous structure consisting of thick, wavy bundles. The medullary cavity of long bones, although usually maintaining its width, may be widened or narrowed (Fig. 3). The trabeculae in the direction of the lines of stress are organized into thick tracts, frequently widely spaced, with intervening connective tissue. The tracts of bone are exaggerations of the stress trajectories seen in normal bones. The bones subjected to vertical stress, such as the vertebral bodies and the ends of the straight long bones, have exaggerated vertical tracts. In other bones where the distribution of forces is more complex, such as at the proximal end of the femur, the calcaneus, pelvis, and scapula, the thickened trajectories are arranged along the lines of stress counteracting the forces of tension and compression (Fig. 5; and 9, *A* and *B*). Thus, two main systems of trajectories crossing each other at right angles are arranged symmetrically around the neutral axis.

Radiolucent Form. This form is seen most frequently in the calvarium of the skull where it is known as osteoporosis circumscripta. It represents the destructive stage of the disease and, if followed for a sufficiently long period of time, it can be observed to change to the mixed and sclerotic forms. The initial lesion usually begins in the frontal or occipital areas, and, over a course of years, spreads slowly to involve the entire calvarium (Fig. 10, *A–D*). The process is usually continuous, extending almost equally to both sides, but it may involve only one side, or arise as separate foci at different locations. The diploë is diminished in density and obliterated or converted to a mesh of fine trabeculae. The outer table is thinned from within. The suture lines do not hinder progress of the disease and are eventually obliterated. The interface between diseased and normal bone is sharply demarcated with no evidence of reactive sclerosis. In time, sclerotic deposits of bone are formed at the sites which were involved earliest and may advance in the same direction and rate as the preceding destructive process. In some skulls, the normal bone, zones of radiolucency, and zones of beginning sclerosis are adjacent to each other. The sclerosis is greatest near the inner table where it may form a continuous layer adjacent to the brain. Other irregular patches appearing in the diploë are in sharp contrast to the surrounding

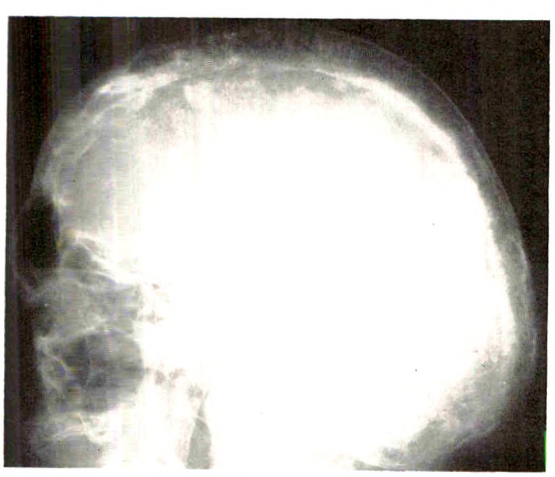


FIG. 11. Predominantly destructive Paget's disease with some patches of sclerosis in the frontal bone. The thickened calvarium is defined peripherally by a thin layer of periosteal bone. Basilar impression has occurred.

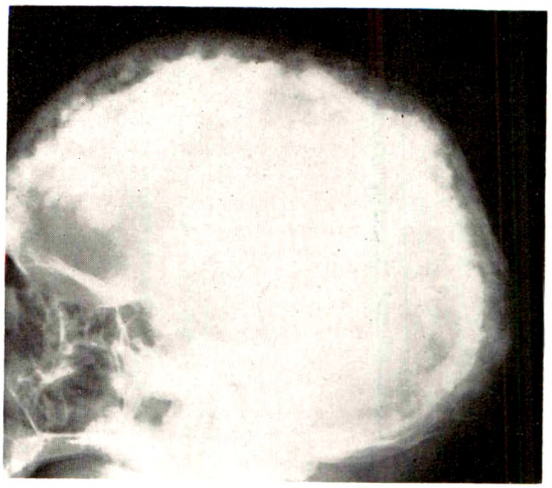


FIG. 12. Dense areas of sclerotic bone scattered throughout the calvarium are more prominent along the inner surface.

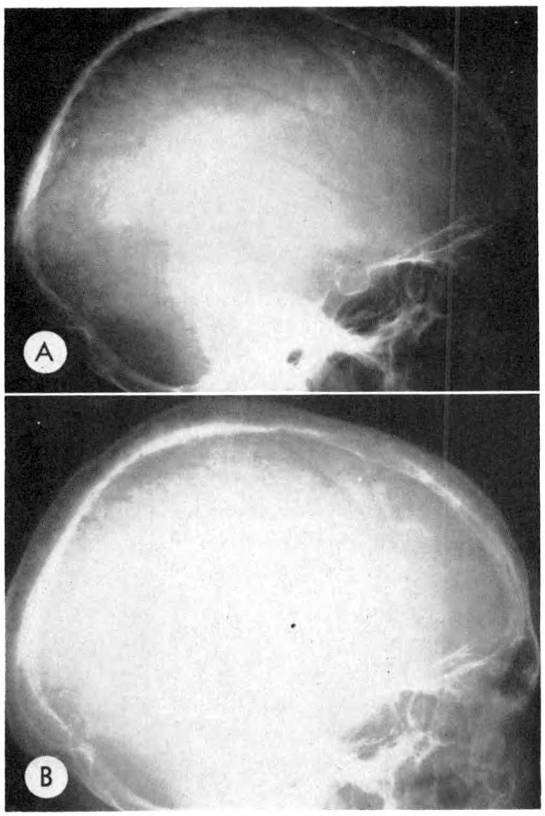


Fig. 13. (*A*) Diffuse demineralization of the calvarium associated with large meningeal grooves. (*B*) Under-exposed roentgenogram to show the smooth thin outer table and slightly thickened calvarium. The inner table is relatively dense.

radiolucent fibrous tissue. At this time the outer table migrates peripherally as a result of bone apposition on the periosteal surface and attrition on the diploic surface, resulting in a markedly thickened cranium. The thin outer subperiosteal layer is always present, although it may not be visible on the roentgenogram unless a bright light is used to view it, or unless the film has been underexposed (Fig. 11; and 13*B*).

As the destructive process subsides, new bone forms on the inner surface of the external bony plate, eventually replacing the connective tissue and producing a thick, dense outer table. The disease is then quiescent and no further alterations occur (Fig. 12).

Occasionally, the entire calvarium may be involved by the destructive process with no evidence of new bone formation visible except for a thickening of the calvarium from periosteal proliferation. The appearance may be similar to that of osteoporosis, or may differ only in the greater thickness of the skull. Some cases present a mottled radiolucency.[7] In 1 case of diffuse demineralization, the grooves for the meningeal vessels were large, possibly the result of large vessels feeding the vascular diseased bone (Fig. 13*A*).

In the long bones, extensive destructive lesions without evidence of repair is not common. Cases have been reported in which a cyst-like lesion involved the anterior superior part of the tibia[3,4,21] or other long bones. These lesions are initially spindle shaped with the cancellous bone reduced in

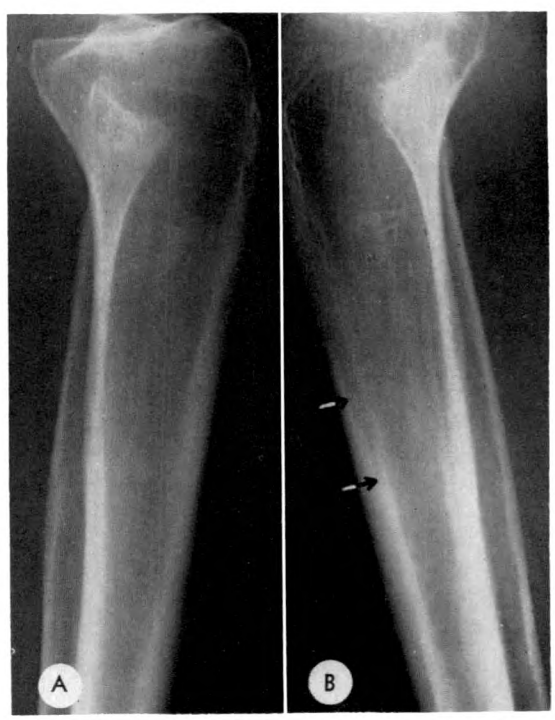


Fig. 14. (*A*) Normal left tibia. (*B*) Destructive lesion involving the anterior compact bone and the spongiosa of the upper third of the right tibia. The compact bone is less dense and the almost homogeneous shadow is replaced by vertical striations, presumably the result of widening of the haversian spaces. The lower border is sharply demarcated from normal compact bone in the shape of a V (arrows). The vertical trabeculae of the spongy bone are thickened.

density and the homogeneous compacta being replaced by parallel layers of spongy bone. The advancing margin is surrounded by normal bone, clearly defined in the form of a V (Fig. 14, *A* and *B*). The outer surface may be a thin layer of bone deposited by the elevated periosteum. As the lesion grows, it retains its V-shape at the periphery. This configuration differentiates it from other types of lytic lesions.

Paget's disease begins at one end or both ends of a long bone and progresses toward the other end. By studying the advancing edge of the lesion on roentgenograms, one can reconstruct the sequence of events leading from the active destructive lesions to the thick, sclerotic, healed phase. Immediately adjacent to the normal bone is an area of diminished density involving, predominantly, the center of the cortex. Longitudinal striations representing enlarged haversian canals are present (Fig. 15).

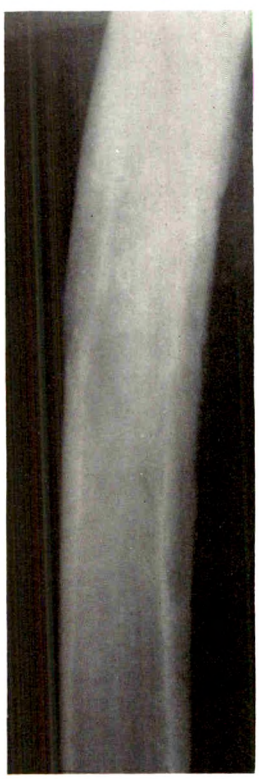


Fig. 15. Lateral roentgenogram of the femur. The destructive, sharply demarcated lesion is seen best in the posterior cortex. Vertical striations are now visible in the cortex.



Fig. 16. Active, progressing lesion of the distal tibia. The margin is sharply demarcated in V shape. The periosteum has formed a thin layer of bone, expanding the shaft. The older lesion is situated proximally. All stages in the development of Paget's disease can be seen with the sclerotic healing phase visible at the top of the roentgenogram. More proximal in the tibia, but not illustrated, the radiolucent tissue beneath the thin periosteal layer has been replaced by dense Paget's bone.

Schmorl[20] observed that this was the result of osteoclastic resorption of the haversian canal walls and their subsequent replacement by vascular connective tissue. By observing the adjacent, more extensively involved bone, it is apparent that, as the lesions approach the periosteum, a thin layer of periosteal lamellar bone is formed and expansion occurs. A bright viewing light is sometimes necessary to see this newly formed bone on the roentgenogram. The radiolucent marginal lesion and elevated periosteal new bone are indicative of still active and progressive lesions. With healing, as seen farther along the diseased



FIG. 17. This patient had bilateral symmetric fractures involving the lateral cortex of the proximal femoral shafts, seen on earlier roentgenograms. A residual scar was present in the left femur and the fracture in the right femur has some beginning endosteal and periosteal callus. Due to the fact that the bones were demineralized and had bilateral symmetric horizontal defects, and that the patient had an elevated serum alkaline phosphatase, she was treated unsuccessfully for osteomalacia. It is believed that this disease can be differentiated from osteomalacia because (1) the cortical defects involve the lateral surface of the femur, the usual site in Paget's disease but not in osteomalacia; and (2) the trabeculae along the lines of stress are thickened in the left femur.

shaft, the fibrous tissue becomes converted to bone; the periosteal bone thickens from within and ultimately is incorporated into the thickened cortex (Fig. 16).

Some cases present a generalized demineralization of a bone indistinguishable from that of osteoporosis. The trabeculae along the lines of stress thicken and form prominent trajectories which are usually more pronounced in Paget's disease (Fig. 17) than in osteoporosis, although in osteoporosis, too, the trabeculae may be thickened along the stress lines. Unless roentgenograms of other parts of the skeleton have been obtained, uncertainty about which of the two diseases is present may arise. Paget's disease, unlike osteoporosis, ordinarily involves only a part of a bone or a limited part of the skeleton (Fig. 18, *A* and *B*). Both diseases, however, occur in elderly people and are frequently associated with each other. We have had 2 patients with Paget's disease, both of whom also had thinning of the parietal bones of the skull, a condition probably related to osteoporosis.[26]

Vertebrae involved by lytic lesions may resemble hemangiomas because of the presence of thick vertical trabeculae. In these cases, similar involvement of the neural arch, spinous process, and transverse processes, or of other bones, is usually present, a condition not seen in hemangioma. The destruction of bone may be so extensive that no trabeculae will be visible within the vertebral body (Fig. 19, *A* and *B*).

The diffusely demineralized bones of the lower extremity, without thickening of the cortex, may also resemble those in osteoporosis. One patient with such diffuse demineralization of the pelvis and femora

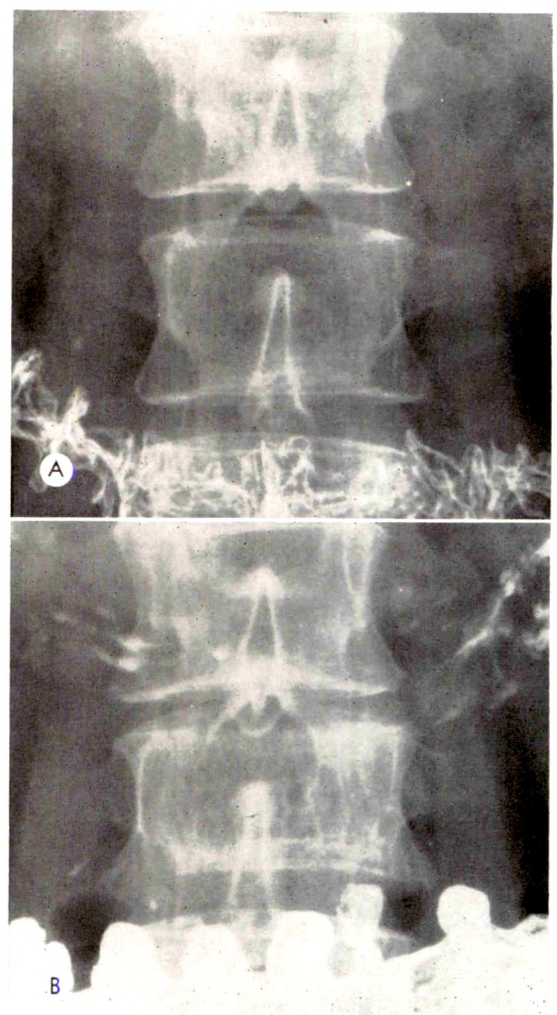


FIG. 18. (*A*) The third lumbar vertebra is less dense than the adjacent vertebrae. The pedicles are partially obscured, particularly on the left. (*B*) Three and one-half years later the typical coarse vertical striations of Paget's disease have appeared.

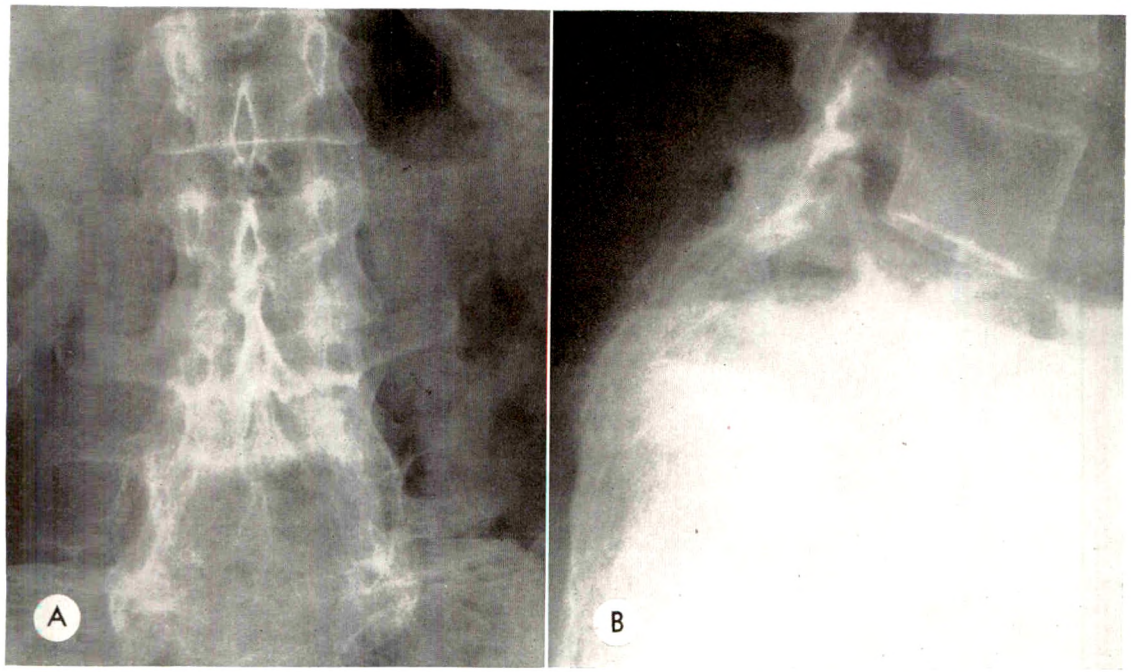


Fig. 19. (*A* and *B*) There is almost complete destruction of the fourth and fifth vertebral bodies; this had been noted for several years, diagnosed as hemangioma, and treated with roentgen irradiation. The presence of typical Paget's disease in the neural arches, attached processes, and in the sacrum, suggesting that the destruction was due to this disease, was substantiated by biopsy.

sustained a fracture of the neck of the right femur; bone biopsy revealed Paget's disease. Roentgenograms of the femur after open reduction showed the typical horizontal defects of the lateral cortical surface representing healed fissure fractures (Fig. 20, *A* and *B*). These lesions, when present, establish the diagnosis of Paget's disease.

A severe osteolytic form may occur, frequently involving only one tubular bone, in which the bone is rapidly destroyed, even the cortex disappearing in some areas. Expansion and deformity develop with striations extending in many directions (Fig. 3).

It has been stated that the articular cartilage is not involved by Paget's disease.[4,7,20] However, in cases with unilateral involvement of the pelvis or of the head of one femur, the articular cartilage adjacent to the bony abnormality frequently is narrow (Fig. 5). On the roentgenogram, the cartilage narrowing usually appears uniform throughout and is frequently not associated with hypertrophic changes. It is possible that the narrowing results from accelerated endochondral ossification with enlargement of the bone and replacement of part of the deeper layers of cartilage by Paget's bone. If this is true it could contribute to the elongation of tubular bones. Schmorl[20] observed a similar narrowing between the intervertebral disks and adjacent involved vertebrae and at the margins of the costal cartilage in Paget's disease as well as in osteomalacia and hyperparathyroidism. Others[13,24] observed the same phenomenon in acromegaly, where articular cartilage proliferation is associated with subchondral new bone formation.

Jaws and Teeth. Contrary to the opinion of some early investigators,[18,20] the disease frequently is present in the jaws.[22] Stafne[22] found it at this site in 23 of 138 cases of Paget's disease. The maxilla was involved in 20 and the mandible in 3. In 19 of the 23 cases, the skull also showed abnormality.[23]

The earliest change observed is a demineralization, which may be uneven, of the

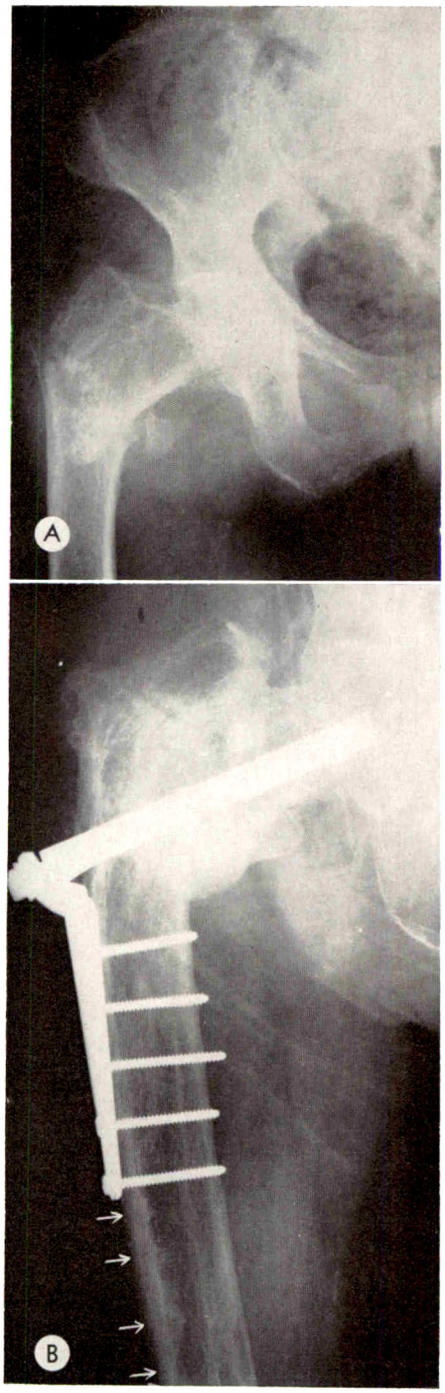


FIG. 20. (*A*) Intertrochanteric fracture of the right femur associated with diffuse demineralization of the pelvis and both femora. Slight thickening of the stress trajectories, but this is no greater than that seen in some cases of osteoporosis. A biopsy of the fracture site at the time of open reduction showed Paget's disease. (*B*) Roentgenogram obtained after surgery includes the mid-shaft of the femur, which was not seen on the preoperative roentgenograms. Typical healed Paget's clefts are visible in the lateral cortex below the metallic plate.

bone around the teeth. The trabeculae bearing the stresses of the teeth may become thickened giving a fibrillar pattern. The lamina dura disappears and the cementum and dentine about the apices of the teeth are resorbed.[6] Since the cementum is a thin shell of modified bone tissue covering the dentine of the root and neck of a tooth, it is not surprising that it also is destroyed by a disease affecting adjacent bone.[16] In some cases, the radiolucent lesions about the roots of the teeth resemble apical abscesses but the teeth are not carious and show no evidence of infection (Fig. 21). In later stages the bone becomes sclerotic, as in other parts of the skeleton, and the lamina dura does not reappear. Hypercementosis replaces the resorptive lesion, producing a bulbous enlargement of the root of the tooth which may be ankylosed to the surrounding bone.

SUMMARY

Paget's disease is primarily one of bone destruction. In the reparative phase, excess bone is formed which produces a characteristic roentgen appearance. In some cases, the long, persistent, destructive phase presents problems in roentgen diagnosis, particularly if the disease is diffuse and is present in patients who also have osteoporosis. The destructive phase of the disease can be diagnosed if: (1) the characteristic fissure fractures or their residual clefts are present in the long bones of the lower extremities; (2) the margin in compact bone can be seen to be sharply demarcated and, sometimes, associated with a thin layer of subperiosteal new bone; or (3) the trajectories formed along the lines of stress are thickened. Characteristic destructive lesions frequently are seen in the skull and about the roots of the teeth.

Bone apposition on the convex surface or

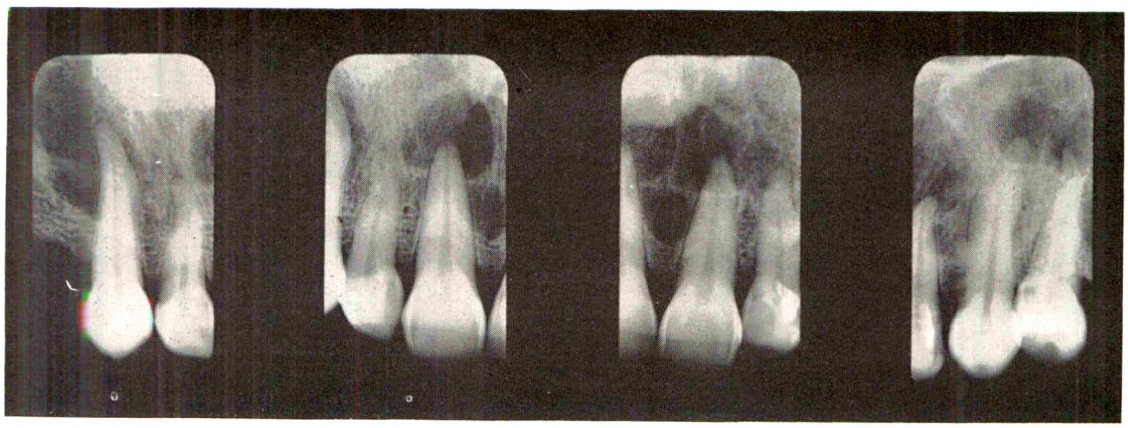


Fig. 21. Sharply demarcated destructive lesions about the roots of several upper teeth. Thick trabeculae of the surrounding bone. (Reproduced with permission of the Year Book Publishers, from "Endocrinology in Clinical Practice," 1953, p. 98.)

the surface subjected to tensile forces produces thickening of a bone. This may be followed by resorption resulting in bending of the bone without reducing its length.

The activity of the disease can be assessed by its roentgen appearance.

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EARLY CHANGES IN CHARCOT'S JOINTS*

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THE roentgen appearance of advanced Charcot's arthropathy has been well documented and presents little difficulty in diagnosis. However, the changes observed in the incipient stages of this lesion may constitute a problem in diagnosis for the radiologist and the clinician. The difficulties in the diagnosis of the evolving Charcot's joint become self-evident when it is realized that tabetic arthropathy may develop as a presenting symptom before other signs and symptoms of disease of the central nervous system are present. Twenty per cent of patients with Charcot's joints show no additional signs of cranial nerve or spinal cord disease, while serologic examinations of the blood and cerebrospinal fluid are negative in approximately 50 per cent of patients with tabes dorsalis.[15] Since treatment may be effective in arresting progress of the destructive joint lesions, recognition of the process in its early stages should contribute to more satisfactory functional salvage. Earlier recognition, as in any disease, will often spare the patient painful and usually fruitless procedures undertaken as therapeutic measures or for the purpose of establishing a diagnosis.

This paper will discuss the roentgen findings in early Charcot's arthropathy as noted in 5 cases reviewed by the authors. Although the diagnosis of neurosyphilis was established in all but 1 of these patients, the roentgen studies were misleading.

PATHOGENESIS

The actual causative factors in the development of the articular lesions are not established. Charcot believed that the etiologic mechanism was either damage to trophic centers in the spinal cord or degeneration of the peripheral nerves. Volkmann and Virchow, on the contrary, regarded trauma as the major exciting cause. Eloesser,[2] seeking to evaluate trauma as the primary force, demonstrated that typical neuropathic joint disease did not develop if only the dorsal roots in laboratory animals were severed. If, however, the anesthetized joints were subjected to direct trauma, neuropathic joint lesions were produced.

It is often stated that the Charcot joint is painless.[1] However, during the early phase of joint effusion pain is frequently present.[9] In a study designed to explain the paradox of pain in the anesthetic joint, Eloesser[2] thrust pins into experimentally produced Charcot's joints in cats. Observing that the soft tissues around the joint were extremely sensitive, while the bony surfaces and periostium were not, he concluded that soft tissue distention by the effusion was the factor which produced pain.

EARLY ROENTGEN FINDINGS

In the early stages of the disease, the roentgen findings have been reported as those of joint effusion, subluxation, various forms of degenerative bone changes and spontaneous fractures.[1,11,14] Each change may exist separately or in association with others. There is no definite chronologic order of appearance. Since severe Charcot's arthropathy may develop within several weeks, roentgen studies may not be done early enough to record incipient changes.[5] However, most cases progress slowly and in these the roentgen signs of early lesions are most apt to be observed; the roentgen interpretation must be accurate inasmuch as it may provide the only clue to the presence of the process.

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JOINT EFFUSION

Joint effusion is a common early change.[1,10,13,14] It may occur spontaneously or following a slight trauma and it varies from a mild hydroarthrosis to one of massive proportions (Fig. 1). Distention of the joint with separation of the articular surfaces is seen. The bony contours remain regular and well defined. Aspiration of the fluid is invariably followed by recurrence. A characteristic of this effusion is its chronicity and persistence.[10] The effusion is attributed to simple transudation from the vessels.[12] Trauma, enhanced by impaired sensory perception, may result in hemorrhage into the joint, adding to the volume of an effusion.

An actual increase in the mucin content of the synovial fluid may be found. This is associated with proliferation of the synovial cells and is followed by hyperplasia and thickening of the joint capsule. The capsule may become extremely thick and bulky, retaining a large amount of fluid. Capsular rupture may ensue.[6]

CASE I. A fifty-two year old Negro female was hospitalized because of pain, numbness and tingling of the lower extremities and difficulty in walking of eighteen years' duration. Approximately twenty-five years earlier she had been treated for syphilis. Neurologic examination revealed tabes dorsalis and serologic studies of the blood and spinal fluid were positive for syphilis. There was swelling and crepitation of the right knee joint.

The initial roentgenogram was interpreted as showing minimal "hypertrophic" changes and extensive joint effusion (Fig. 1*A*). Two days later there was marked increase in the effusion and enormous distention of the joint. The patella was markedly displaced by the effusion and there was slight medial subluxation of the femur on the tibia (Fig. 1, *B* and *C*). Re-examination five years later demonstrated a typical, advanced Charcot's joint (Fig. 1*D*). The patient had refused arthrodesis when first seen and had not returned for further treatment.

Comment. Although the clinical findings in this patient were readily recognized as those of tabes dorsalis, the roentgen changes were interpreted as those of hypertrophic osteoarthritis. The significance of marked effusion into the joint was not appreciated.

SUBLUXATION

Subluxation is probably related to generalized muscular hypotonia. With loss of synergistic reflexes and sensory loss, the muscles and ligaments remain the sole factors in the maintenance of joint alignment and stability. When they become overstretched, subluxation takes place. Effusion also contributes to the development of subluxation by stretching the ligaments, which become increasingly relaxed. Abnormal joint alignment takes place (Fig. 1, *B* and *C*). This in turn results in faulty weight bearing with excessive stress upon the articular surfaces and is followed by destructive changes.

CASE II. A fifty-three year old white male was treated for tabes dorsalis in 1939. Roentgenograms of the left knee revealed mild joint effusion with no abnormality of the bony architecture or joint surfaces (Fig. 2*A*). Seven months later there was a decrease in the height of the joint space at the medial aspect, sclerosis of the tibial articular surface, and increased joint effusion (Fig. 2, *B* and *C*). Fourteen months later there was further loss in stature of the joint space and increased sclerosis of the articular surfaces of the tibia and femur; amorphous, dense, calcific debris representing typical advanced disease were present in the joint space and the joint effusion had become even greater (Fig. 2*D*).

Comment. This case illustrates the more slowly developing type of Charcot's joint. Here the lesion in its early evolution cannot be distinguished roentgenologically from hypertrophic osteoarthritis.

BONE CHANGES

The osseous changes in the neuropathic joint are similar, pathologically, to hypertrophic osteoarthritis. In fact, some authors even deny the existence of a true neuropathic joint, maintaining that this is but a severe form of osteoarthritis.[14] Since Charcot's joint occurs in those age groups in which hypertrophic osteoarthritis is also widely prevalent, the differentiation of the lesions may be very difficult. The problem is

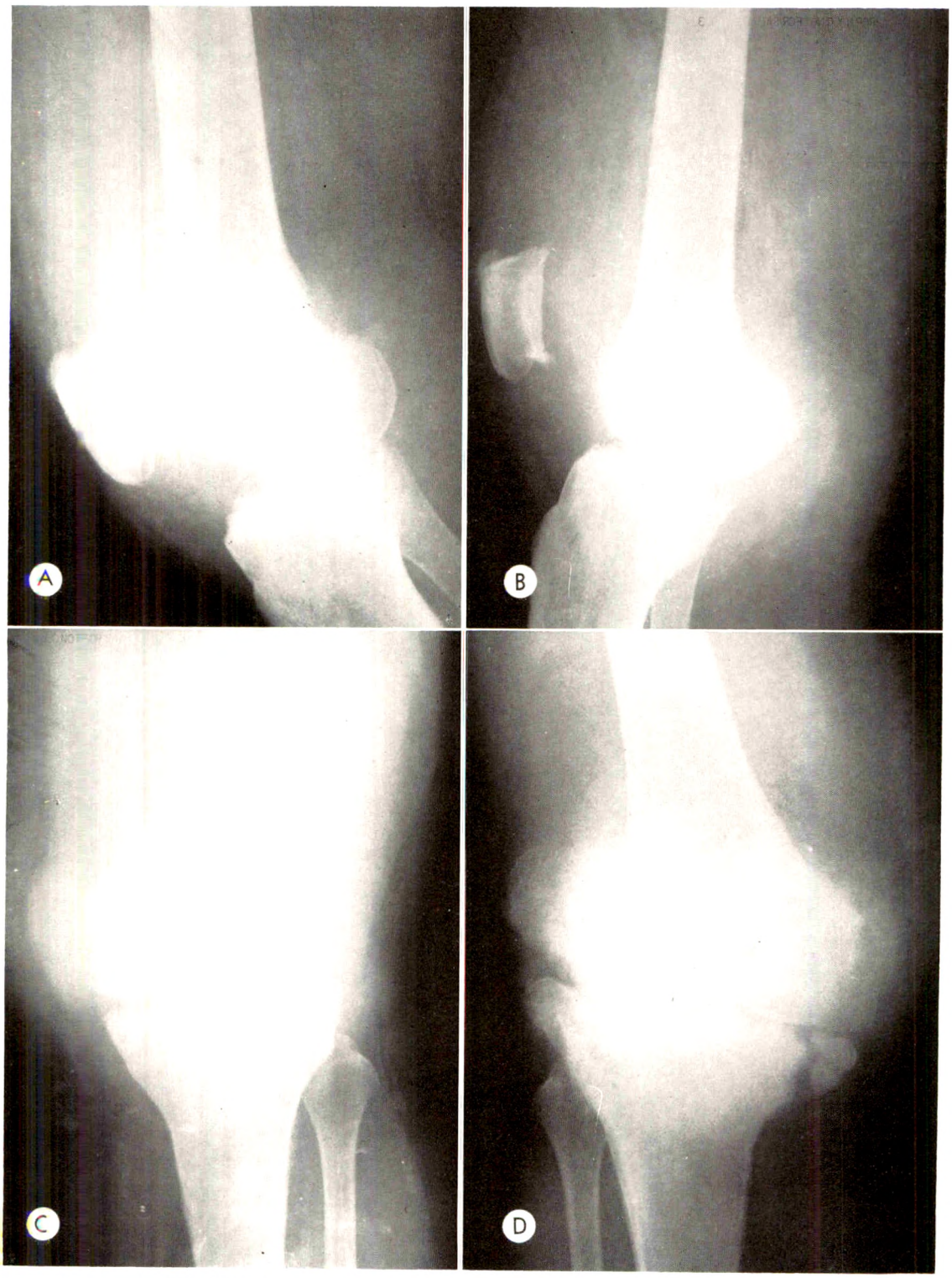
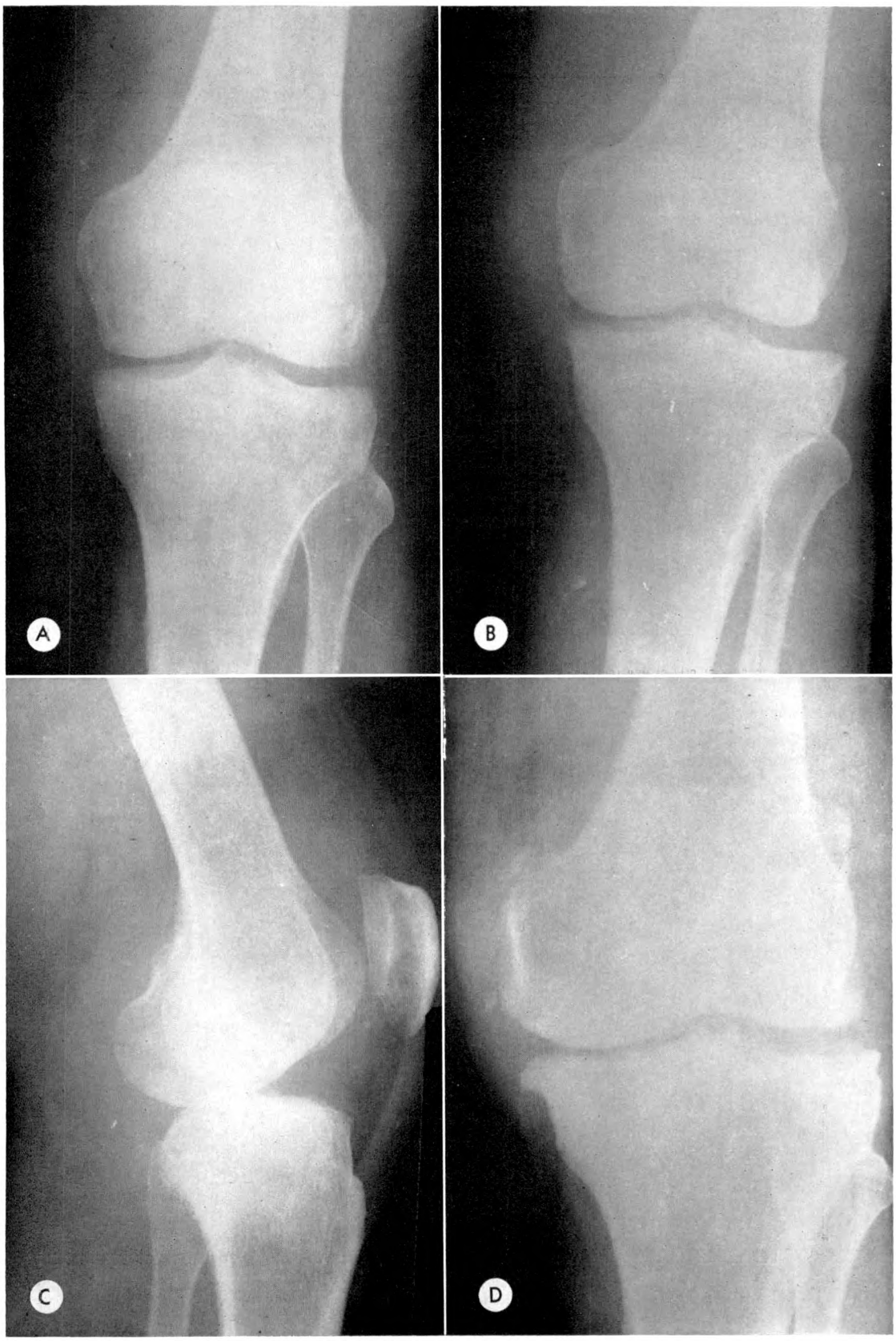


Fig. 1. Case 1. (*A*) The initial roentgenogram shows minimal "hypertrophic" changes and extensive joint effusion. (*B* and *C*) Two days after *A* there is marked increase in the effusion with enormous distention of the joint. The patella has been markedly displaced by the effusion and there is slight medial subluxation of the femur on the tibia. (*D*) Typical advanced Charcot's joint five years later.


A
B
C
D

further complicated by the fact that both diseases may be present simultaneously.

Microscopically, also, neurotrophic changes resemble those of osteoarthritis. There is degeneration and partial disappearance of the articular cartilage. The collagenous fibers are exposed and show fibrillation. Granulation tissue in the form of a pannus grows over the articular cartilage, eventually invades it, and begins to absorb it. In the neuropathic joint this pannus is more active and profuse than it is in osteoarthritis. When areas of cartilage are fully destroyed, the exposed bone begins to proliferate and produce new bone. This is a reactivation of the process of endochondral bone formation which takes place in growing bone, and it accounts for the roentgen finding of sclerosis beneath surface defects. At the periphery of the joint this active bone formation gives rise to marginal osteophytes.[5,9]

Horwitz[5] observed that bone and cartilage debris are ground into the synovial membrane early in the evolution of Charcot's joint. This feature of the microscopic pathology of the disease enabled him to establish the diagnosis in 5 patients in whom there were no definite clinical or roentgen findings of neuroarthropathy. Similar microscopic findings were present in 19 cases of advanced tabetic arthropathy, whereas in a control series of 30 joints involved by other types of arthritis there were only 2 instances in which bone and cartilage debris were found in the synovial membrane, both of the latter being far advanced osteoarthritic lesions. Horwitz[5] thus concluded that this histologic finding indicated neuroarthropathy, and was particularly useful in recognition of the early lesion and its differentiation from other types of joint disease.

Roentgenologically, diffuse sclerosis may be the earliest finding (Fig. 5*A*). The bony trabeculae are obscured and a slight increase in bone density is evident.[3,7] These changes are attributed to deposition of calcium within the interstices of the bone.[1] When the articular cartilage is destroyed, irregularities and erosions of the bony cortex are seen (Fig. 3*A* and 4*A*). Irregular, patchy areas of sclerosis may then become evident. The early osteophytic formations in Charcot's joint are said to differ from osteoarthritic spurs only by their unsharp outlines and rounded fuzzy margins, which tend to merge with the surrounding soft tissues.[6] They present a somewhat bizarre appearance and may attain enormous size and break off.

Case III. A fifty-seven old white male was hospitalized because of an incapacitating limp of the lower extremity and pain in the left hip. Five years previously he had been treated for syphilis. Serologic studies of the blood and spinal fluid were consistently negative for syphilis, although physical examination showed tabes dorsalis. Roentgen study on admission revealed moderate sclerosis of the acetabulum and an early destructive lesion of the head of the right femur (Fig. 3*A*). The left hip was already extensively destroyed, presenting typical roentgen findings of Charcot's arthropathy. Re-examination during a second admission five months later showed advanced destruction of the right femoral head characteristic of late Charcot's neuroarthropathy (Fig. 3*B*).

Comment. The lesion in the right hip, representing incipient Charcot's disease, was indistinguishable in its roentgen appearance from hypertrophic osteoarthritis. Despite characteristic findings of severe Charcot's arthropathy in the left hip, the initial changes of a similar lesion in the right hip were regarded as "degenerative." Attention was focused on the severely damaged left hip to the neglect of the right

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Fig. 2 Case II. (*A*) Roentgenogram of the left knee reveals slight joint effusion. The bony architecture and joint surfaces are normal. (*B* and *C*) Seven months later there is a decrease in the height of the medial aspect of the joint space and slight sclerosis of the tibial articular surface. The joint effusion has increased. These changes are indistinguishable from those of hypertrophic osteoarthritis. (*D*) Fourteen months later there is further reduction in the joint space and increased sclerosis of the articular surfaces of the tibia and femur. Dense amorphous calcific debris is present in the joint space indicating advanced disease. The joint effusion has also increased considerably.

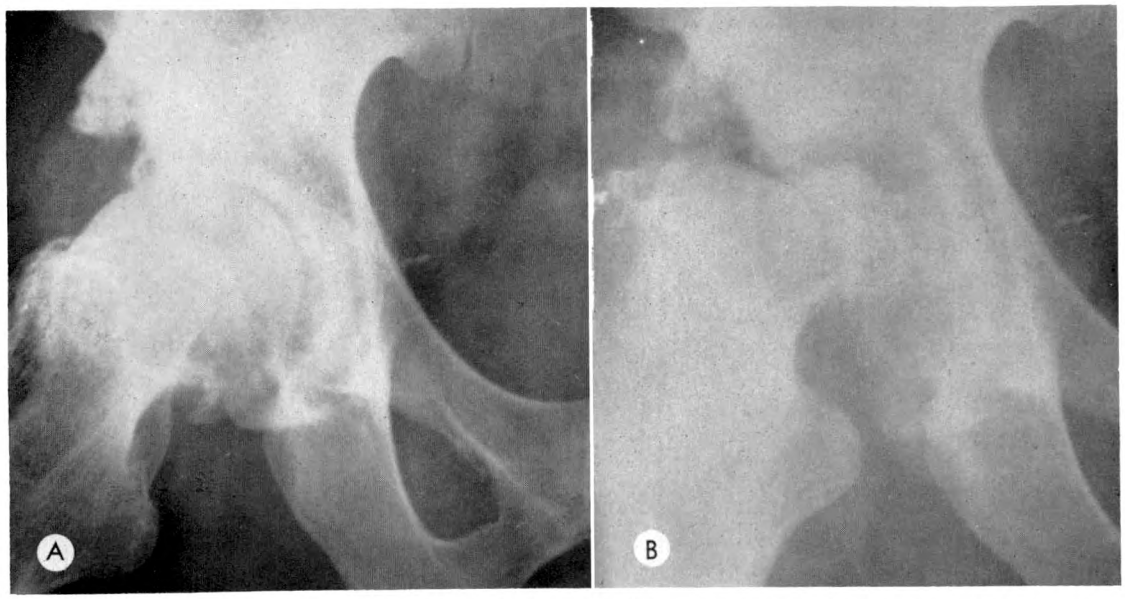


FIG. 3. Case III. (*A*) Roentgen study of the right hip reveals moderate sclerosis of the acetabulum and an early sclerotic lesion in the head of the right femur. (*B*) Re-examination five months later reveals severe destruction of the femoral head. The amorphous calcification within the joint space and the dense bone sclerosis of the involved femoral head are characteristic of the late changes in Charcot's joint.

which, thereafter, became almost totally destroyed within a five month period. The patient offered no complaints regarding his right hip. These changes illustrate the early roentgen findings in the evolving Charcot's joint.

CASE IV. A fifty-six year old white male was hospitalized for treatment of hypertensive heart disease and congestive heart failure. Diagnostic studies included a roentgenogram of the abdomen which revealed an abnormality of the right hip. Further roentgen study disclosed narrowing of the joint space, sclerosis of the acetabulum and cyst-like areas of radiolucency and mottled areas of sclerosis producing deformity of the femoral head and neck (Fig. 4*A*). The findings were interpreted as those of osteoarthritis. The patient had no complaints referable to the right hip and he was discharged after recovery from his congestive heart failure.

Re-examination four months later, when the patient was readmitted primarily for a complaint of pain in the right hip area and weakness of the right lower extremity, revealed advanced destruction of the femoral head and considerable calcific debris in the distended joint space (Fig. 4*B*). On the basis of these roentgen findings the diagnosis of Charcot's joint was suggested, although there was no supporting evidence in the history, physical findings or laboratory studies. Numerous examinations of the blood and spinal fluid and repeated neurologic examinations failed to provide evidence of syphilis. In an effort to establish a diagnosis and rule out neoplasm, two surgical biopsies were performed but neither revealed the true nature of the lesion.

Two years later the patient had a spontaneous fracture at the proximal intercondylar portion of the right tibia. This was entirely unrelated to trauma or sprain, was painless and was manifested by severe ecchymosis of the leg and knee. Until roentgenograms disclosed the fracture, the lesion was diagnosed as a "local subcutaneous hemorrhage probably due to blood dyscrasia." Finally, after a period of more than two years from onset of the articular lesions, the diagnosis of syphilis in this patient was established by tests for *Treponema pallidum*.

Comment. This case illustrates the elusive nature of the diagnosis of Charcot's joint in its incipient phase. Early, the lesion simulated the commonly observed roentgen findings of hypertrophic osteoarthritis. Later, even characteristic roentgen findings of neuropathic joint disease were not recognized because of lack of historical, clinical or laboratory evidence of syphilis. Finally, a spontaneous fracture was interpreted clinically as a local hemorrhagic

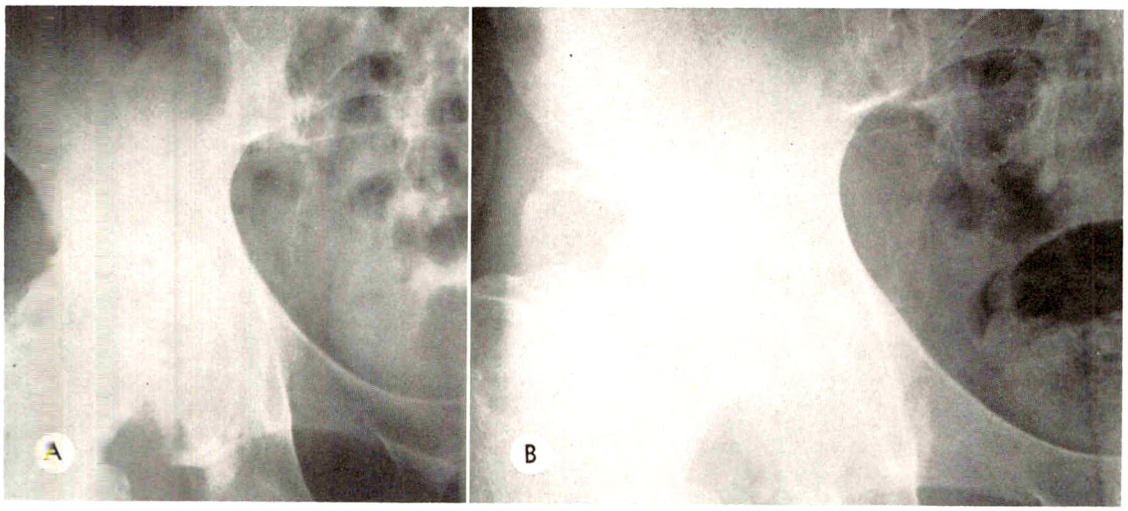


FIG. 4. Case IV. (*A*) Roentgenogram of the right hip shows narrowing of the joint space, sclerosis of the acetabulum and cyst-like areas of radiolucency with mottled areas of sclerosis producing deformity of the femoral head and neck. These changes were interpreted as due to osteoarthritis. The patient had no complaints referable to the right hip area. (*B*) Roentgenogram of the same hip four months later, when patient was readmitted primarily for a complaint of pain in the right hip and weakness of the right lower extremity, reveals advanced destruction of the femoral head and considerable calcific debris in the distended joint space. On the basis of these findings the roentgen diagnosis of Charcot's joint was suggested although there was no supporting evidence in the history, physical findings or laboratory studies.

manifestation of a blood dyscrasia and, even when the fracture was demonstrated, it was not immediately associated with the coexisting Charcot's joint.

CASE V. A fifty-six year old white male was known to have acquired syphilis in 1917 but he received no treatment until 1932, when he was given malarial therapy. In 1956 he was hospitalized because of weakness of both legs and difficulty in walking of three months' duration. Neurologic examination revealed tabes dorsalis. Laboratory studies of the blood and spinal fluid were positive for syphilis. Roentgenographic study revealed marked narrowing of the disk space between L-2 and L-3 with sclerosis of the proximal portion of the body of L-3 and the adjacent portion of L-2 (Fig. 5*A*). Two and one-half years later there was marked destruction of the apposing surfaces of the vertebral bodies with beginning development of large osteophytes (Fig. 5, *B* and *C*).

Comment. Despite recognition of the classic clinical signs and symptoms of tabes dorsalis, the early changes in the lumbar spine were regarded as "disk injury or degeneration with secondary arthritic changes." The later changes were attributed to osteomyelitis of the spine with spinal cord involvement. As visualized in the initial study, the changes were entirely consistent with degenerative disease of the intervertebral disk. However, the roentgen appearance of the lesion two and one-half years later, while by itself suggestive of infectious process, could hardly have been interpreted as such in view of the earlier studies which in no manner suggested incipient spinal osteomyelitis.

SPONTANEOUS FRACTURES

Charcot himself first noted the frequency of spontaneous fractures in tabes dorsalis. Sudden fracture is often the first sign of the disease.[13] A fracture may occur without preceding articular changes and prior to the onset of neurologic manifestations.[1,11,14] Typically, these fractures occur in or near a joint with predilection for the femur; the tibia, fibula, radius and ulna follow in order of decreasing frequency. Characteristically, these fractures are transverse, in contrast to the oblique and spiral fractures which follow ordinary trauma (Fig. 6*A*). With good immobilization the fractures may heal well. However, adequate immobilization is usually difficult to achieve because of the neurologic lesion.[8]

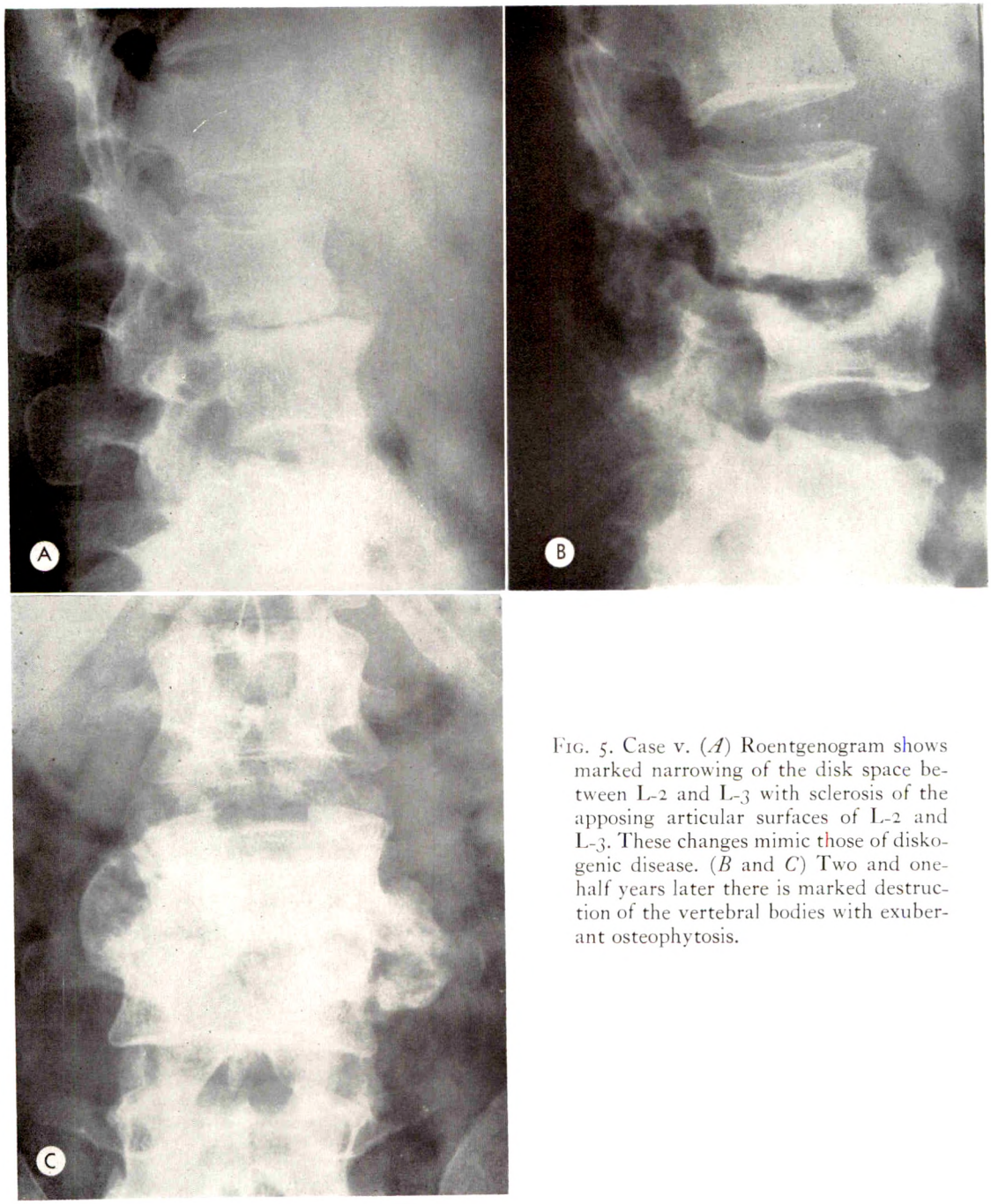


FIG. 5. Case v. (*A*) Roentgenogram shows marked narrowing of the disk space between L-2 and L-3 with sclerosis of the apposing articular surfaces of L-2 and L-3. These changes mimic those of diskogenic disease. (*B* and *C*) Two and one-half years later there is marked destruction of the vertebral bodies with exuberant osteophytosis.

Chemical analysis of the osseous material in the fracture site has demonstrated an actual increase in the inorganic salts. On the other hand, a deficiency of the organic substance has also been observed. Thus, excessive deposition of calcium salts within a poorly developed matrix results in increased brittleness of the bone.[14]

CASE VI. A fifty-six year old white male was treated for syphilis in 1952. Two years later he developed severe "shooting" pains in the lower extremities and difficulty in walking. Two

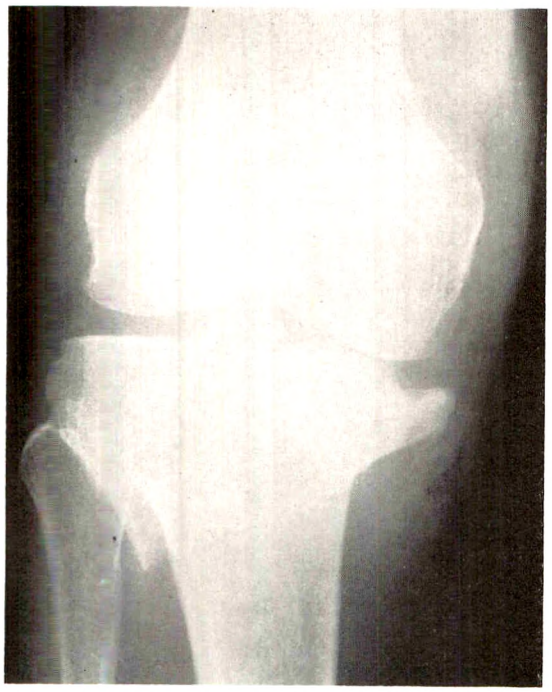


Fig. 6. Case VI. Roentgenogram made eight days following hospital admission reveals a comminuted, transverse fracture of the proximal end of the tibia with depression of the medial plateau. This type of transverse fracture, occurring spontaneously or with relatively minor trauma, is characteristic of Charcot's joint.

years after the onset of these symptoms, his right leg gave way suddenly and spontaneously and he was admitted to the hospital ten days later with a swollen and painful right knee.

Roentgen study performed after the patient had been in the hospital for eight days (eighteen days after the initial episode) disclosed a comminuted, transverse fracture of the proximal end of the tibia with depression of the medial plateau (Fig. 6). Surgical fusion was performed. Blood and spinal fluid remained positive for syphilis.

Comment. Although this patient presented with a history, physical signs and symptoms of tabes dorsalis, the swelling of the knee joint following a simple twisting injury was diagnosed as thrombophlebitis and treated with hot, moist applications and antibiotics. It was not until more than a week after admission that roentgen examination disclosed a fracture which had not been suspected clinically. Even then the fracture was not recognized as a manifestation of tabetic neuroarthropathy. During his hospital stay the lancinating pains in the right lower extremity were attributed to the fracture, although they were recognized later as a symptom of the neurologic lesion. Although this patient had had severe pains in *both* lower extremities, nevertheless there was continued reluctance to classify the fracture of the right tibia as a Charcot's joint. Even the operation for joint fusion was done primarily to control pain, an end which could not be achieved by surgical arthrodesis since the pains were of central nervous system origin.

SUMMARY

In 6 patients roentgen findings representing early changes of Charcot's neuroarthropathy were observed to be: (1) persistent joint effusion; (2) minimal subluxation; (3) degenerative changes of bone manifested by bone sclerosis, erosion and destruction which were difficult to differentiate clinically and roentgenologically from osteoarthritis; and (4) spontaneous fracture unrecognized clinically.

These changes may occur prior to any other clinical or laboratory manifestations of the disease and may masquerade as other lesions of the joints. They are particularly likely to remain unrecognized as manifestations of Charcot's neuroarthropathy.

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CERVICAL DISCOGRAPHY*

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DISCOGRAPHY is a method of introducing radiopaque material directly into a disc preceding the roentgen study. It is relatively new, the first experience being recorded in 1932 by Schmorl and Junghanns.[3] Their report was concerned with lumbar disc injections, which today are routine procedures in many parts of the country. Cervical discography, however, was not attempted until Smith and Nichols[4,5] and Cloward[1] performed it many years later.

ROENTGEN STUDY OF THE CERVICAL SPINE

Previously, roentgen study of the cervical spine was limited to routine roentgenography and visualization of the dural sac by myelography. Cervical myelography, first carried out with lipiodol and later with pantopaque, has both advantages and hazards. The advantages are these: it can be accomplished quickly by fluoroscopy and roentgenography; most of the opaque medium can be removed following the examination; it can be repeated many times; spinal cord tumors or other obstructing lesions of the spinal pathway are easily identified, and medial or lateral disc protrusions can frequently be demonstrated. The chief hazard is that the pantopaque occasionally escapes into the cranial cavity and, once it reaches the cranial subarachnoid space, it is rarely eliminated. The possibility of adverse effect on the central nervous system then may remain indefinitely. Too, this method frequently leads to both false positive and false negative delineations of extradural lesions. The neurosurgeon may consequently perform an unwarranted operation or fail to operate when it is necessary.

CLINICAL FEATURES

When one realizes the number of neurologic syndromes—from amyotrophic lateral sclerosis to hysteria—that the neck and cervical spine can mimic, the necessity of our search for another technique—neurologic, roentgenographic, or otherwise—to assist in clarifying the diagnosis becomes apparent.

When the central nervous system is involved by neck injury or disease in such a way that the examination clearly identifies the location, extent and character of the lesion, the problem is simple. But the neurologic examination, valuable as it is, is usually inadequate by itself to establish a diagnosis that warrants surgical exploration of the neck. False negative or false positive roentgen evidence associated with indefinite neurologic findings further complicates the already difficult diagnosis.

A busy neurologist or neurosurgeon who does not thoroughly pursue the complaints of a partially or totally disabled patient who has few objective symptoms may conclude, despite the many complaints, "I can find no neurologic evidence of cervical spine or neck injury or disease." Had he pursued the patient's complaints more diligently, he might have discovered the nature of the injury or disease. This patient's pain, although it cannot be seen, is real and the muscle spasm and muscle tenderness usually accompanying it certainly indicate a disorder involving the nervous system and may indicate a neck injury or a disease and its extent.

All the structures about a cervical disc may be affected by injury or disease. Each type of injury or disease has a separate and distinct pattern of symptoms. Not only

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may the spinal cord and the peripheral nerves in the neck be affected, but the intrinsic nerve supply to the bones, ligaments, muscles and blood vessels may also be involved. When the latter occurs, these structures become painful irrespective of injury to the nearby spinal cord and peripheral nerves.

The muscle tenderness, pain and spasm frequently present with any joint injury may extend for a distance both proximal and distal to the painful joint. Since the cervical intervertebral space is a joint, being composed of an annular ligament, central nuclear structures, and cartilaginous plates upon the vertebral bodies, it too may be the source of muscle tenderness, pain and spasm.

In spite of a consistent pattern of symptoms identifying the pathologic lesion in the cervical spine, physical findings and those of routine roentgenography and even myelography may be so meager that they cast doubt as to its presence. An additional method of survey which will pinpoint the pathologic process is often necessary, and we have found it in discography.

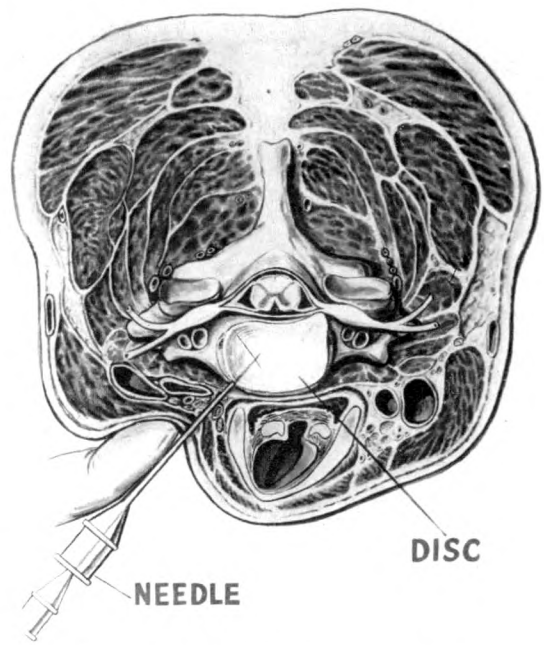


Fig. 1. Drawing showing the needle in place for discography.

Technique of Cervical Discography

Discography (Fig. 1), in contrast to myelography, is an accurate method of evaluating disc derangement. It not only reveals the disc pathology and its extent in detail but it reproduces the symptoms of the patient so that the operator may compare them with the original complaints. In contrast to any other method available at this time, it has demonstrated the highest degree of accuracy in identifying the symptomatic pathologic disc or discs.

To inject a cervical disc, a kit of equipment containing these items is used: three 20 gauge 3 inch needles for making the neck puncture, three $3\frac{1}{2}$ inch 26 gauge spinal needles to inject the disc, two 1 cc. Luer-Lok tuberculin syringes to inject the radiopaque substance into the disc, and one 2 cc. syringe with a hypodermic needle to inject the local anesthetic.

After the skin of the neck is cleansed and antiseptic has been applied, local anesthetic is injected into the skin on the side of the neck. The operator palpates the medial border of the sternomastoid muscle and the carotid artery with his left index finger; the tip of this finger is then passed beneath the trachea and esophagus until the anterior surface of the vertebral column is felt. At this point, if osteophytes are present on the anterior and anterolateral borders of the vertebrae, they can be palpated, and their presence assists in identification of the disc or discs to be injected with the opaque medium.

A needle is inserted into each disc under suspicion until the condition of that disc is ascertained; this is done by passing the 3 inch 20 gauge needle along the left index finger and through the skin and deep structures until it touches a vertebral body or the annulus of a disc. If the operator feels the point of the needle touch the vertebra, he confirms this finding by gently tapping the needle with his finger. The soft tissues are then released and are allowed to "climb back" on the needle. This encounter of the vertebral body with the needle causes the

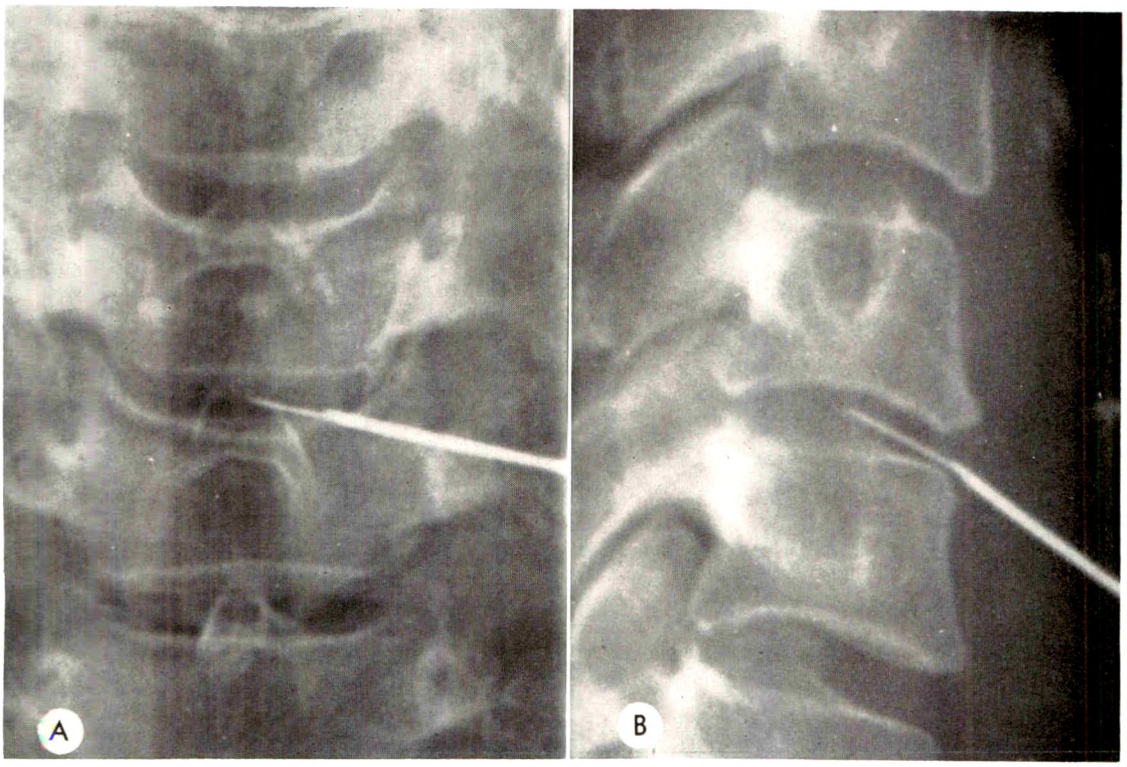


Fig. 2. (*A*) Anteroposterior and (*B*) lateral roentgenograms taken to establish the identity of the disc and the position of the needle.

patient to experience deep pain in his neck at the site of the needle. As the needle is "walked" along the vertebrae, each step causes pain locally in the neck until the annulus of a disc is encountered. Whether the annulus of the disc is encountered before or after the vertebral body, the patient experiences pain in the shoulder blade on the same side.* The operator is assured that the needle is in the annulus of the disc by the evidence of the spread of pain to the scapular area.

The 26 gauge spinal needle is then passed through the 20 gauge needle to the center of the disc. As soon as the 26 gauge needle is inserted, an anteroposterior and a lateral roentgenogram of the cervical spine are taken to establish the identity of the disc injected and the position of the point of the needle (Fig. 2, *A* and *B*). If the needle is not in the proper location, it must be shifted and another pair of roentgenograms taken. At times it may be necessary to do this repeatedly before the position is perfected.

A 1 cc. Luer-Lok tuberculin syringe is filled with 50 per cent hypaque, the stylet is removed from the 26 gauge spinal needle and the syringe is connected to it. Slowly the hypaque is injected. In a normal disc, resistance is felt after the injection of 0.2 to 0.3 cc. of hypaque and this resistance stops the injection, the patient experiencing only a moderate amount of neck and shoulder pain. But pathologically deranged discs will accept from 0.5 to 1.5 cc. of hypaque, and the patient will usually experience immediate extreme pain, numbness and weakness in the head, neck, shoulders, arms and hands.

Because this opaque medium is diffused and absorbed rapidly, the roentgenograms must be taken quickly. The regular roent-

* Cloward[2] has recently reported that the sensory nerve supply to the annulus is by way of the sinuvertebral nerves. These nerves innervate the annulus of the discs in a segmental and unilateral manner. The area of skin reference of the annulus is along the vertebral border of the scapulae.

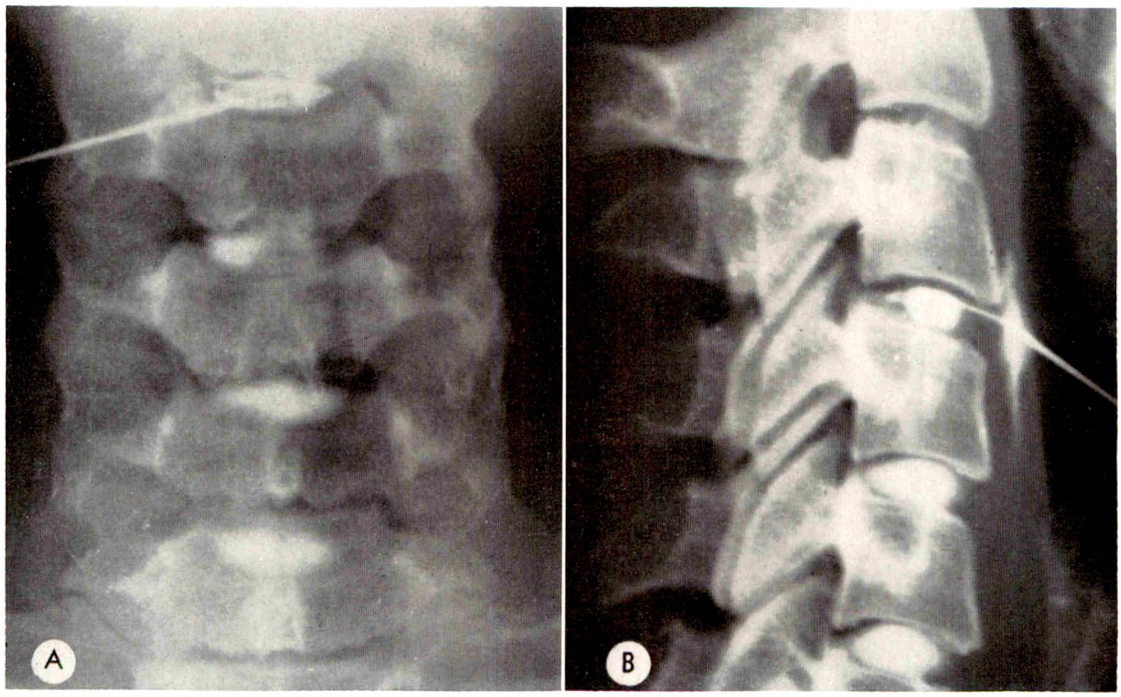


FIG. 3. (*A* and *B*) The disc may be normal with opaque medium concentrated centrally in a globule.

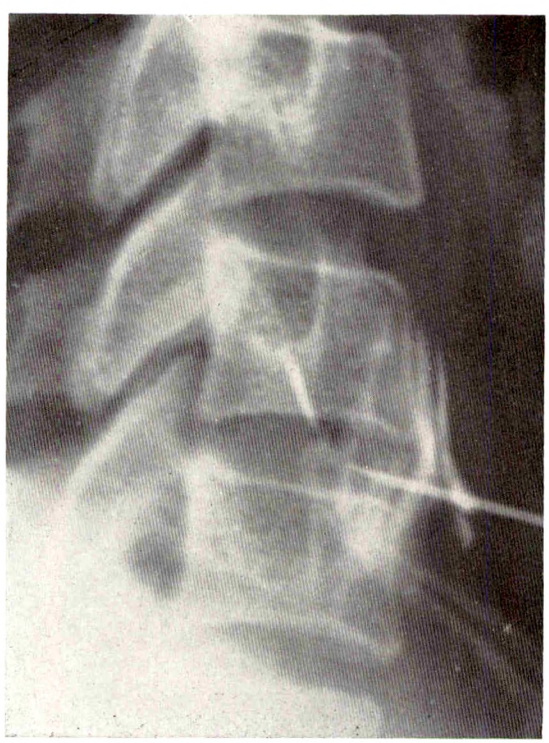


FIG. 4. The disc may be deranged only in an anterior portion.

genographic table with the Bucky diaphragm attached has proved satisfactory. In this case, the lateral roentgenogram is usually taken with a grid; the head unit is ideal for this work because it can be rotated about the neck.

The greatest amount of information is obtained by taking anteroposterior, lateral and oblique roentgenograms of the cervical spine. Additional disc injections should be carried out separately in order to prevent the pathologic findings on the roentgenograms from overlapping.

RESULTS

The purpose of discography is to visualize the derangement of a disc by a roentgen study of the route of the opaque medium through the disc, with particular reference to its point of concentration, the place of its extrusion through the torn annulus and its further spread into the surrounding soft tissues. When the patient experiences a recrudescence of pain, numbness and weakness during the injection, we have identified the symptomatic deranged

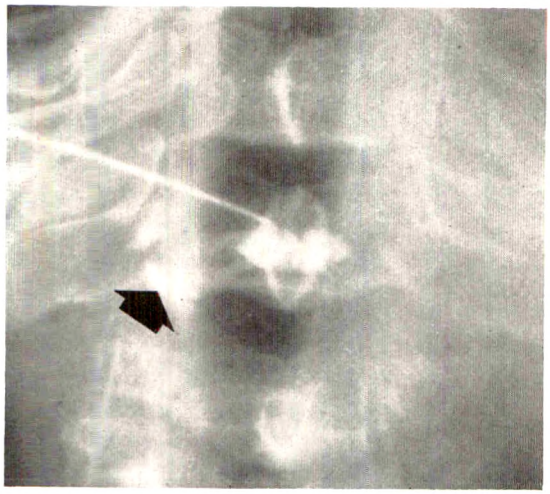


Fig. 5. The derangement may be unilateral.

disc. Damage to the disc can then be estimated and surgical therapy planned.

The discographic survey may reveal *any one* of these conditions: (1) the disc may be normal with the contrast material concentrated centrally in a globule (Fig. 3, *A* and *B*); (2) the disc may be deranged only in an anterior portion (Fig. 4); (3) the derangement may be unilateral (Fig. 5); (4) the entire disc may be severely deranged (Fig. 6); (5) the annulus of the disc may be torn loose from its attachment to the vertebral body (Fig. 7); (6) the annulus may be torn posteriorly or laterally and allow the opaque medium to spill into the adjacent soft tissues (Fig. 8); (7) disc protrusion may be present in the midline anterior

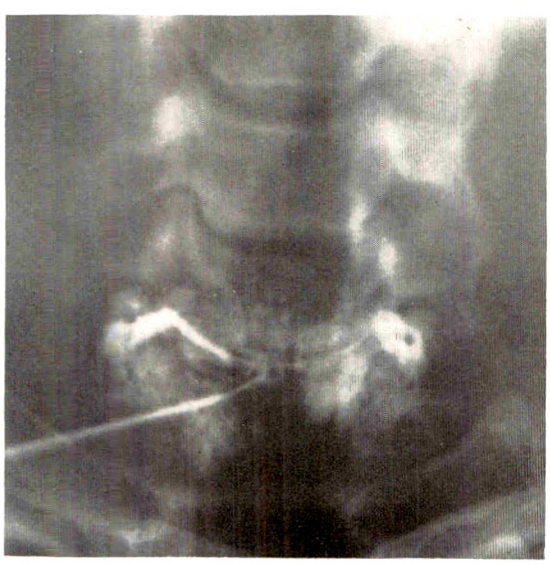


Fig. 6. The entire disc may be severely deranged.

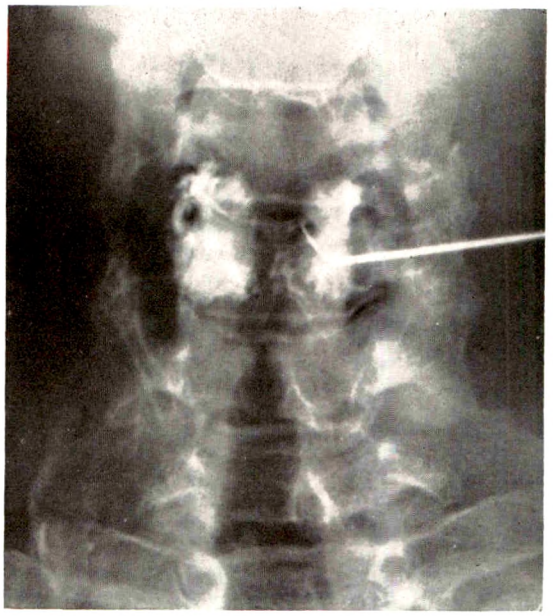


Fig. 7. The annulus of the disc may be torn loose from its attachment to the vertebral body.

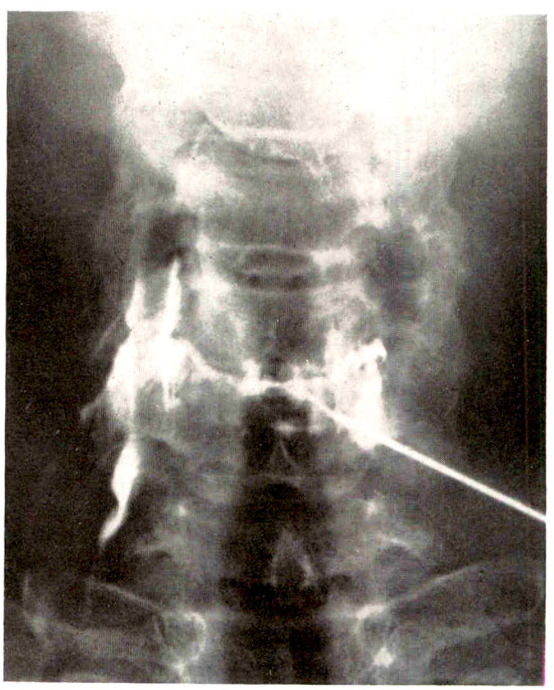


Fig. 8. The annulus may be torn posteriorly or laterally and allow the opaque medium to spill into the adjacent soft tissues.

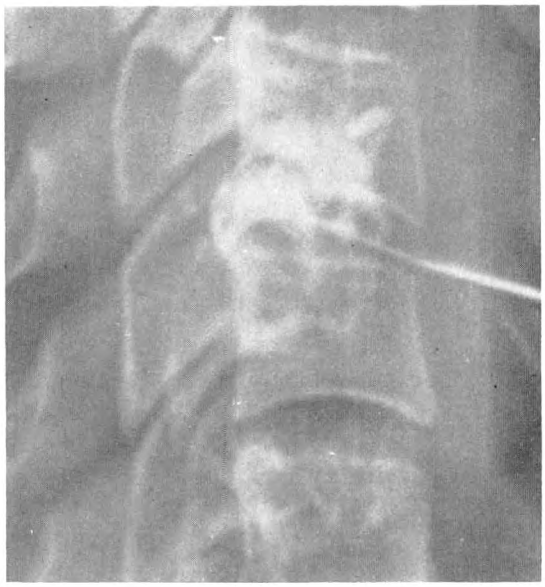


FIG. 9. Disc protrusion may be present in the midline anterior to the spinal cord.

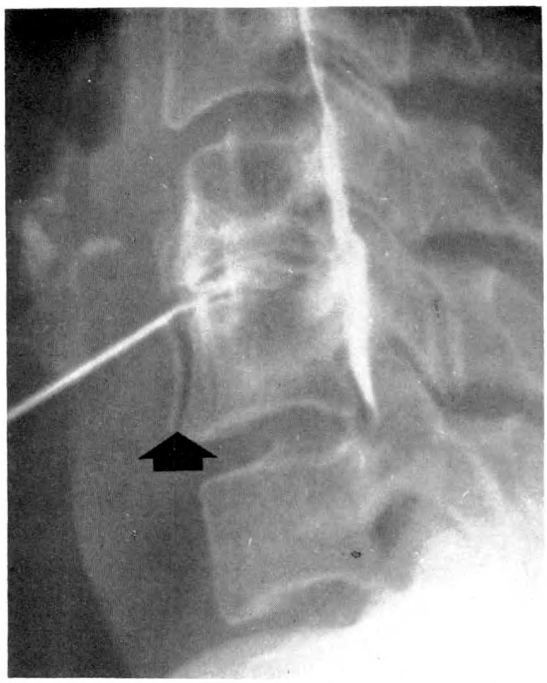


FIG. 11. The anterior longitudinal ligament.

to the spinal cord (Fig. 9); or (8) in the oblique views disc protrusion may be seen in the nerve foramen (Fig. 10, *A* and *B*).

In addition, these anatomic structures may be identified: (1) the anterior longitudinal ligament (Fig. 11); (2) the posterior longitudinal ligament (Fig. 12); (3) the joints of Luschka (Fig. 13); (4) the vertebral cartilage plate (Fig. 14); (5) the dura and epidural space (Fig. 15); (6) the perineural space and nerve root (Fig. 16); and (7) the vertebral artery (Fig. 17, *A* and *B*).

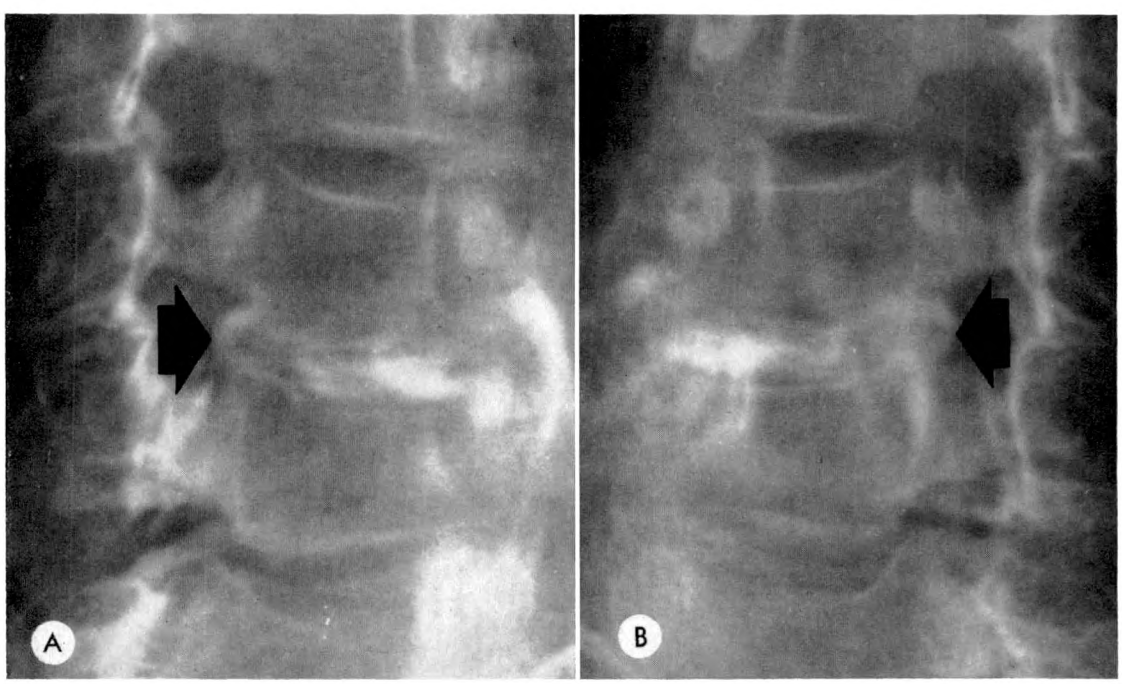


FIG. 10. (*A* and *B*) In the oblique views, disc protrusion may be seen in the nerve foramen.

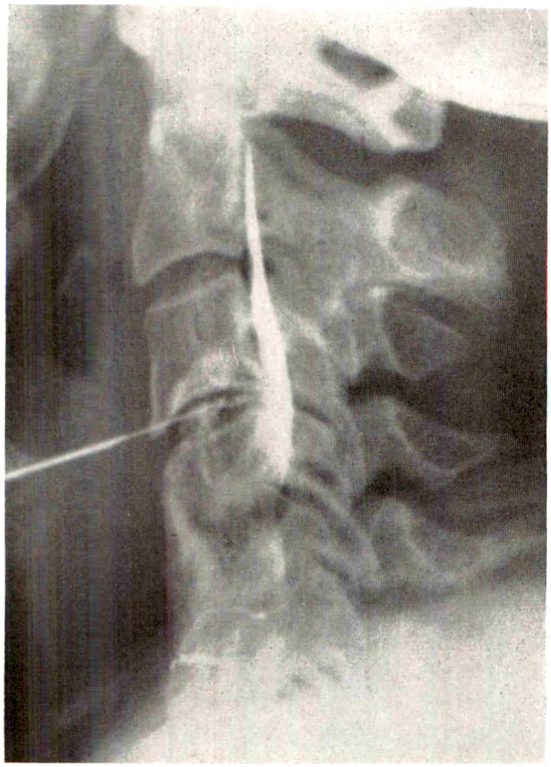


Fig. 12. The posterior longitudinal ligament.

SUMMARY AND CONCLUSIONS

Discography, by demonstrating roentgenographically the internal structures of a disc, identifies both the normal disc and the deranged disc.

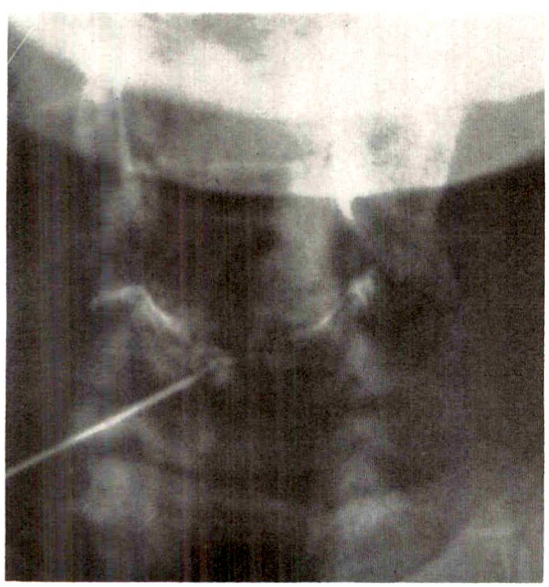


Fig. 13. The joints of Luschka.

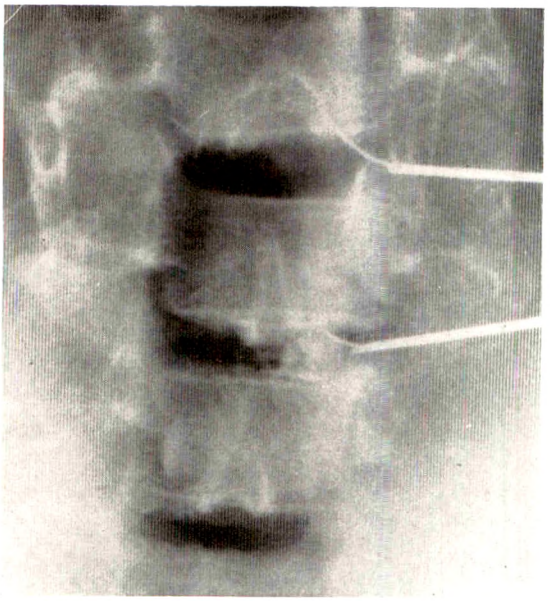


Fig. 14. The vertebral cartilage plate.

Cervical discography is accomplished more easily than cervical myelography and with greater safety. It delineates the normal and the deranged disc so accurately that the type and extent of disc derangement can be seen in detail and the need for disc excision can be readily established.

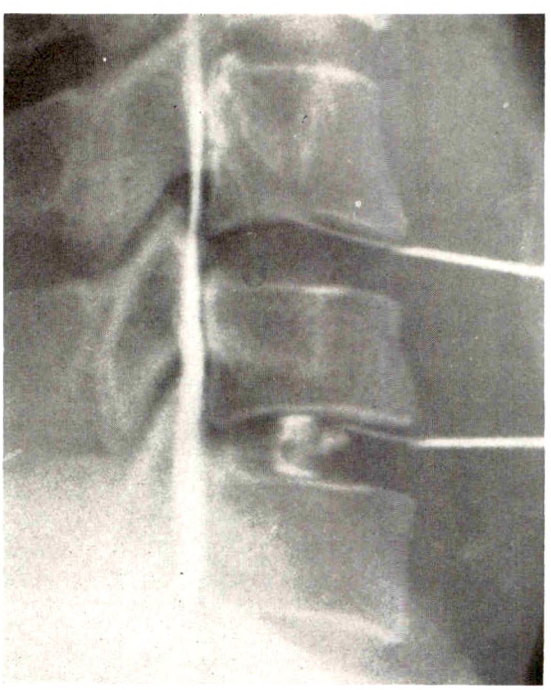


Fig. 15. The dura and epidural space.

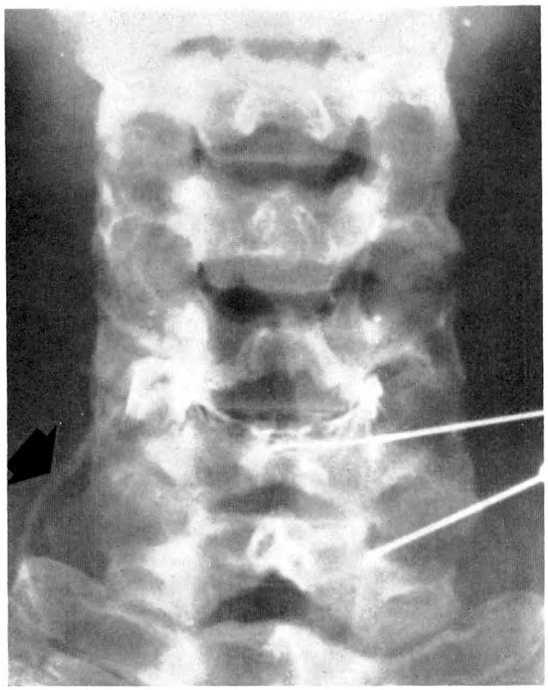


FIG. 16. The perineural space and nerve roots.

Injection of the disc irritates the nerve supply to the disc, the adjacent nerve roots and, occasionally, the nearby spinal cord and causes the patient's symptoms to be reproduced. This evidence assists the surgeon in identifying the pathologic disc needing treatment.

Cervical discography has thus proved to be a major adjunct to the routine roentgenographic study of the cervical spine.

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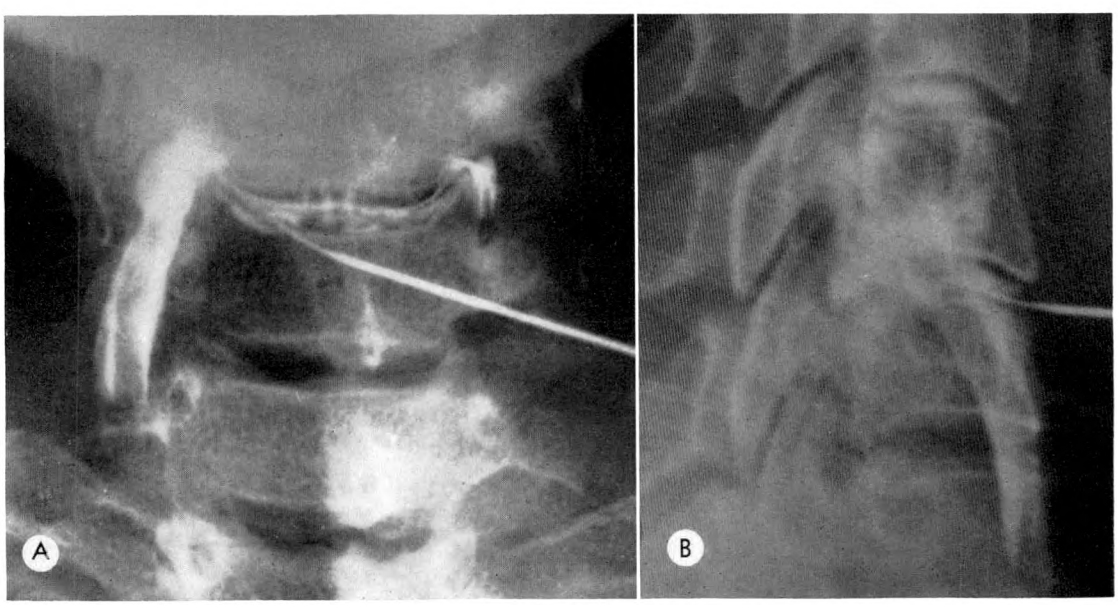


FIG. 17. (*A* and *B*) The vertebral artery.

ISOINTENSITY PATTERNS OF SCATTERED RADIATION AROUND A MIRROR OPTIC PHOTOFLUOROGRAPHIC UNIT*

By JACK M. MORGAN, B.S., *and* RUSSELL WIGH, M.D.
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WITH the development in the last few years of the much faster mirror optic cameras for photofluorographic procedures, exposure dosages to patients have been reduced so that they more closely approach the amounts obtained from conventional chest roentgenography. These newer cameras also play an important role in the protection of technical personnel. An investigation of the scattered radiation around a modern photofluorographic unit containing a mirror optic system has been carried out; it shows a considerable reduction compared with previously published results when lens type cameras were employed.[1,2]

EQUIPMENT AND PROCEDURE

Radiation measurements were made around a 70 mm. straight hood (type X-70S) Fairchild-Odelca camera. The working aperture is f.0.8. The camera and roentgen-ray tube are supported as one single unit so that vertical movement of one results in the same movement of the other. The collimation of the primary beam was aligned by placing roentgen-ray films at the camera surface 40 inches from the target. Exposures made in this fashion permitted correction of an original malalignment and ensured that the primary beam was confined to the fluoroscopic screen surface of the camera and hood.

The position of the chest survey unit in the relatively small lead lined examination room is demonstrated diagrammatically in Figure 1. The equipment is controlled from behind a protective barrier located in one corner of the room. The tube is operated at 90 kv. peak and 150 ma. with the exposures phototimed. The roentgen-ray beam is filtered with 2.5 mm. of aluminum. The film used is Kodak Photoflure, PFG 469, green sensitive.

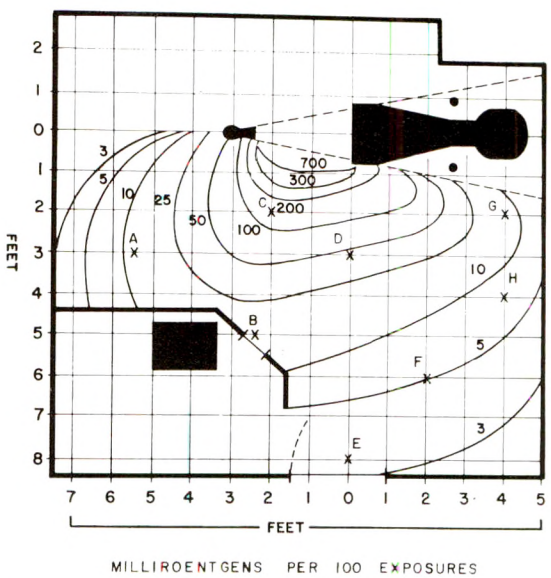


FIG. 1. Isointensity curves, indicating the distribution of scattered radiation around a mirror optic photofluorographic installation.

Measurements were made with Victoreen Model 362 pocket ionization chambers and with a .025 r Victoreen chamber. The pocket chambers were selected for non-leakage and a linear response of from 0 to 200 mr; they were found to be accurate within 2 per cent of full scale when tested with a standard radium source.

Figure 2 illustrates the arrangement of a number of chambers. The small chambers were spaced at 6 inch intervals on a portable stand. This stand was readily moved to various positions throughout the room. It allowed a large number of measurements to be made simultaneously. The active vol-

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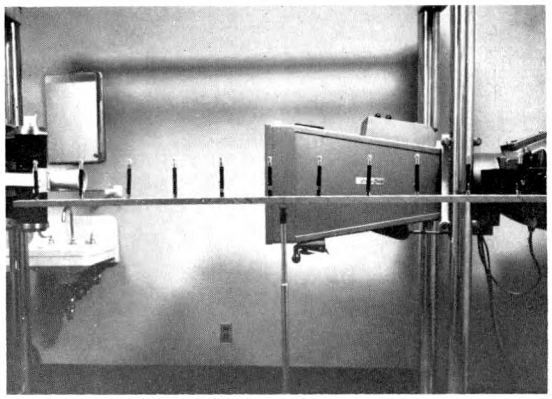


FIG. 2. An adjustable stand holds pocket ionization chambers near a 70 mm. straight hood photofluorographic unit.

umes of the chambers were adjusted to the same plane as that of the horizontal beam during each exposure. Measurements of scattered radiation were obtained both from patients and from a tissue equivalent masonite phantom. The phantom gave an exposure equivalent to that of a patient with a chest measurement of 22 cm. at the nipple line. Most of the measurements carried out for the isointensity patterns were obtained using the phantom. From measured points of equal intensity, isodose curves were constructed and are shown superimposed on the room layout (Fig. 1). The curves are expressed in milliroentgens per 100 exposures.

DISCUSSION

Morgan and Lewis[1] working with a 35 mm. camera and Van Allen[2] employing 70 mm. cameras, all of the lens type, have published isodose curves for such installations. Our isointensity patterns show a reduction in scatter of major degree. Although the phantoms that these investigators used were in each instance equivalent to a patient 2 cm. larger in chest diameter than ours, this is not considered to be a significant factor. Undoubtedly, the faster present day films do play a part in the observed differences, but the major change is related to the difference in camera speeds.

The experiments also differ in the sizes of the rooms used. Our data were accumulated in a room one-seventh the size of the rooms of the other investigators. Therefore, our measurements include backscatter from the walls to a much greater degree.

If one selects random points at equal distances from the equipment, the reduced scatter using the mirror optic camera is impressive. Table 1 compares the scatter at such points of measurement for the two types of cameras.

TABLE I

SCATTERED RADIATION USING DIFFERENT PHOTOFLUOROGRAPHIC CAMERA SYSTEMS
(in mr/100 exposures)

Points of Measurement	Lens Optics		Mirror Optics
	Morgan and Lewis[1]	Van Allen[2]	Present Authors
A	70	250	14
B	40	110	14
C	320	350	150
D	80	200	40
E	10	30	3
F	12	30	5
G	10	200	12
H	12	40	7

At only one of these points does the radiation in the mirror optics data exceed that of the lens systems. Figure 1 indicates that this point is close to a wall. It is probable that backscatter accounts for the high value.

Values for areas outside of the room and in the control section were much less than 1 mr per 100 exposures. The walls of the room and of the protective barriers around the control contain 1/16 inch of lead.

SUMMARY

Measurements made around a modern chest photofluorographic roentgen-ray installation utilizing a mirror optic system indicate less scattered radiation compared with that from lens type photofluorographic cameras.

A diagram shows a typical installation of a mirror optic type camera with its field patterns of scattered radiation.

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EXPERIMENTAL OPACIFICATION OF ORGANS AND STRUCTURES TO ROENTGEN RAYS*

By F. R. STEGGERDA, PH.D.,† *and* CESARE GIANTURCO, M.D.‡
URBANA, ILLINOIS

IN 1937 the authors described a method for the permanent roentgen visualization of the colon based on the infiltration of its walls with particulate opaque material.[4] This method proved useful for physiologic studies of the colon in animals.

In recent years, devices capable of subjecting animals to high acceleration or deceleration have been developed in connection with space programs, and some of the men in charge of the medical aspects of these programs have been interested in the displacement of various organs and structures during such stresses. These displacements are usually studied by strapping the animals to high velocity sleds and taking instantaneous roentgenograms at the moment of maximum deceleration. Some of these studies were not satisfactory because of insufficient roentgenographic contrast, and the authors were requested to supply a number of dogs in which organs had been made opaque to roentgen rays. Therefore, the purpose of the following experiment is somewhat unique, but the methods employed are susceptible of ordinary physiologic applications and are reported for this reason.

MATERIAL AND METHOD

Thirty-one dogs were prepared. The organs opacified were the liver, spleen, colon, stomach, duodenum, short loops of small bowel, urinary bladder, kidneys, diaphragms, and the pericardium.

Visualization of the liver and spleen was achieved by the intravenous administration of thorotrast. All other procedures required opening the abdominal or thoracic cavity under general anesthesia. After isolation of the organ or structure to be visualized, a suspension of a particulated sterile opaque material was introduced just under the outer surface by using a No. 26 needle to make multiple small injections about 1 cm. apart. Following this, the wound was closed and the animal was allowed to recover.

The opaque substances which were used were thorotrast (Testagar Company, Detroit, Michigan) and micronized barium sulfate (Micropaque) (Damaney and Company, Ware Hertz, England). Thorotrast was found to be very suitable for organs without a rich lymphatic network, such as the colon and the kidney capsule. When the lymphatic network was well developed,

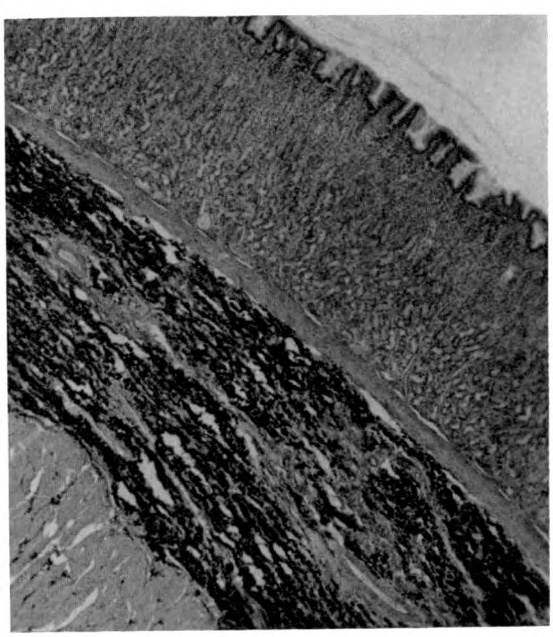


FIG. 1. Macrophages laden with thorotrast particles in the submucosa of the colon of a dog.

* Work done for U.S.A.F. contract number 29-(600)—2038.
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‡ Section on Radiology, Carle Hospital Clinic, Urbana, Illinois.

thorotrast was carried away before it could become fixed by the tissues. In such cases, micronized $BaSO_4$ proved to be a more satisfactory medium because it has larger particles which are not easily dispersed by the lymph vessels.

All animals prepared did well postoperatively. Roentgenograms taken soon after surgery showed a rather patchy distribution of the opaque substance, but a more even opacification was usually evident ten to twenty days later. This was especially true in the colon where the eventual appearance recalls that achieved by double contrast examinations.

Several dogs were sacrificed for gross and histologic studies at various times following surgery. All organs were grossly normal. On microscopic study, the opaque material was found to be imbedded in large macrophages. In the gastrointestinal tract most of these barium and thorotrast laden macrophages were concentrated in the submucosal layer (Fig. 1). The type of tissue reaction was essentially the same for thorotrast and $BaSO_4$.

Fourteen of the 31 animals were kept under observation for more than ten months,

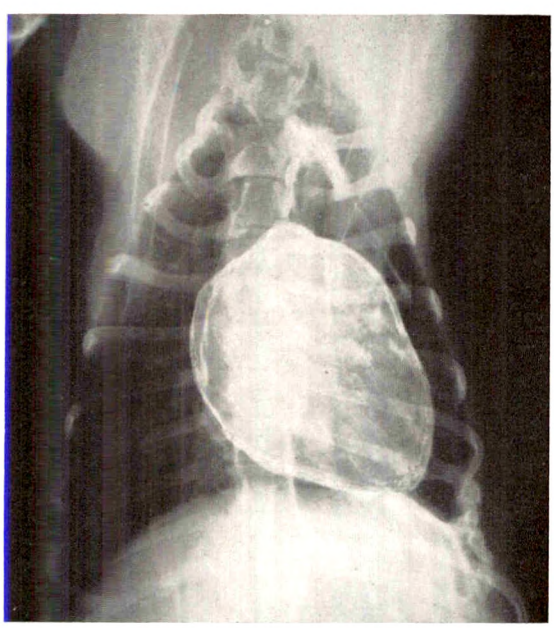


FIG. 2. Thorotrast in the pericardial wall of a dog.

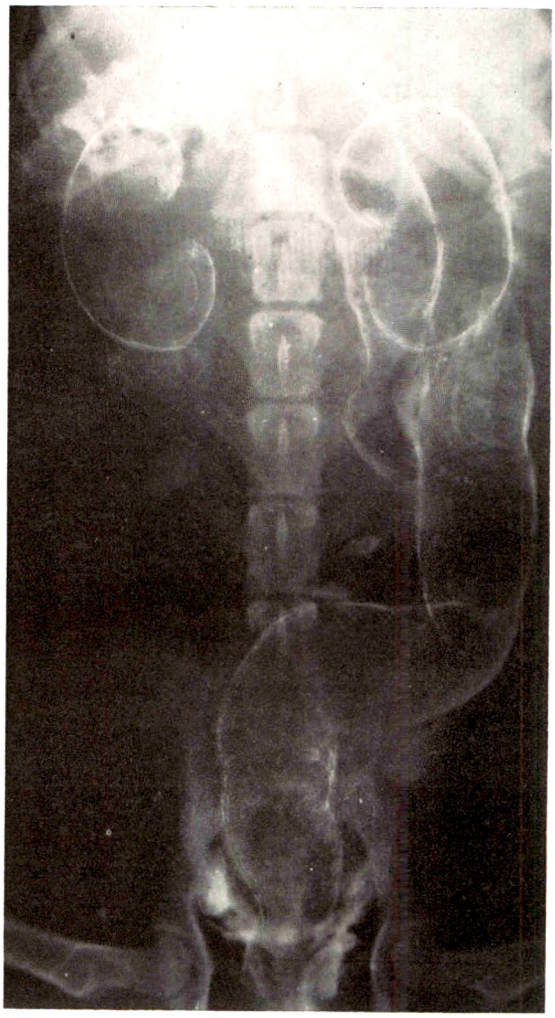


FIG. 3. Thorotrast in the kidney capsules and in the wall of the left colon of a dog.

and all of them appeared to remain in excellent health. The illustrations show the quality of the images obtained (Fig. 2, 3, 4, and 5).

PHYSIOLOGIC APPLICATIONS

The physiologic applications of this method of opacification are manifold. In hollow muscular organs, the proper roentgenologic technique will reveal contractile patterns under normal conditions and under the influence of various stimuli, regardless of the presence and of the volume of the contents of the organs and without the misleading effects of anesthesia. In the

parenchymal organs, volume changes can be estimated from the changes in the size of their roentgen shadows. In some cases this may take the place of plethysmographic studies, which usually involve surgical exposure of the organs and general anesthesia.

CONCLUSIONS

As a general conclusion it can be stated that thorotrast and finely divided particles of $BaSO_4$ can be used in experimental animals to make permanently opacified to roentgen rays such organs as the colon, stomach, small intestine, urinary bladder, kidney, diaphragms and pericardium.

Thorotrast, a medium that is highly miscible with body fluids, has proved to be a very desirable medium for the opacification of some organs. Micropaque (finely ground $BaSO_4$) can be used as a substitute for thorotrast in other organs where the lymphatic drainage is such that thorotrast is drained away. $BaSO_4$ is not distributed in the tissues as well as thorotrast is and it gives an appearance of patchiness.

Thorotrast carries the stigma of being radioactive and therefore possibly damaging to body tissues over a period of time.[3] Histologically, the presence of thorotrast or $BaSO_4$ in the walls of an organ will produce an infiltration of macrophages, but the severity of this response is not great and does not seem to interfere with the basic physiology of the organs.

It is believed that organs permanently opacified to roentgen rays can be used for studying physiologic responses for a year or more after the material is injected.

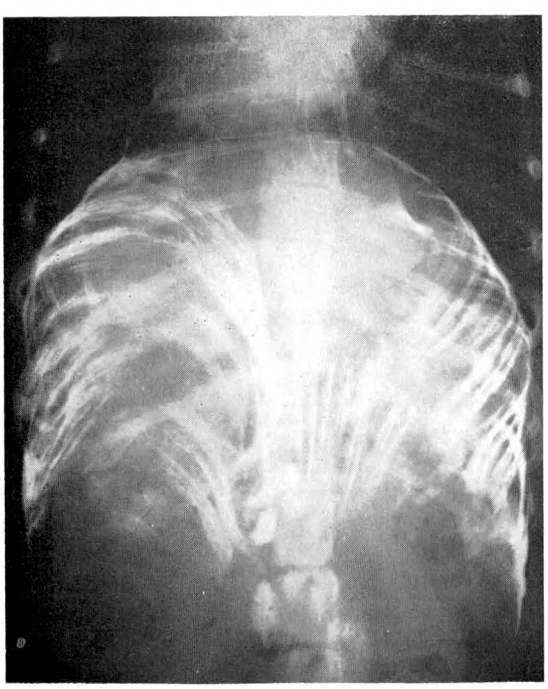


FIG. 4. $BaSO_4$ in the diaphragm of a dog.

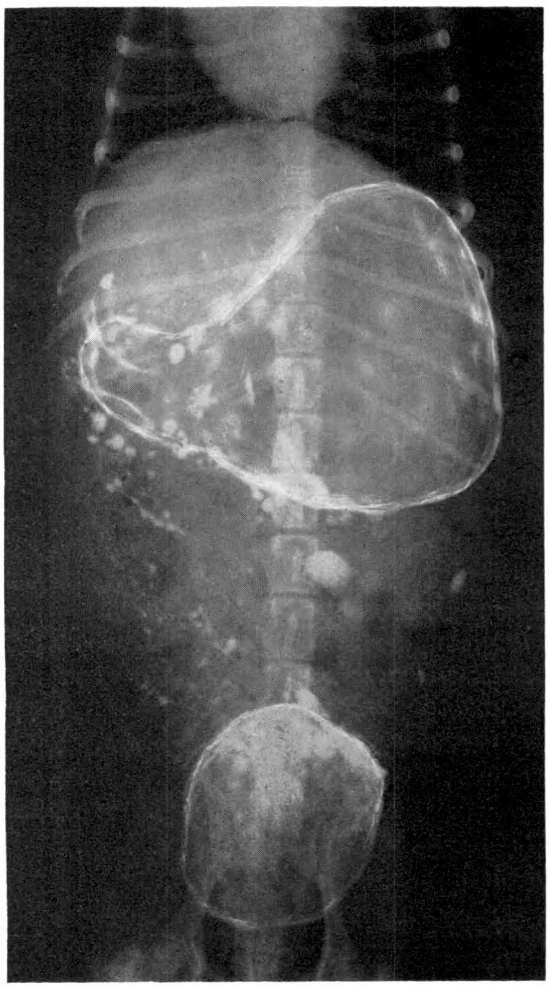


FIG. 5. $BaSO_4$ in the stomach wall and in the wall of the bladder of a dog.

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EDITORIALS

THE SIXTY-SECOND ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

THE Sixty-second Annual Meeting of the American Roentgen Ray Society was held at the beautiful Deauville Hotel, Miami Beach, Florida from Tuesday, September 26 through Friday, September 29, 1961.

President Harold O. Reineke issued the call to order and then introduced Dr. W. L. Fitzgerald, President of the Dade County Medical Association and Clinical Professor of Urology at the University of Miami, Florida, who delivered an Address of Welcome in which the example of scientific informational interchange embodied in this meeting was lauded. The transcendation of national boundaries and elevation of ideals above pursuit of personal aggrandizement was set forth as a model of cooperation for international diplomats and statesmen. The Society was most cordially greeted in the name of the 1,400 members of the Dade County Medical Association.

President-Elect Traian Leucutia was then installed in the office of highest honor. Dr. Ralph M. Caulk, Chairman of the Executive Council, awarded the President's Medal, and President Reineke presented two gavels; the first, a symbolic one fashioned from the tooth of a mastodon and recovered from Alaskan glacial ice, and the second, the working gavel fashioned from mementos representing the contributions of Röntgen, Coolidge and Snook to radiology.

The Inaugural Address by President Leucutia titled, "Integrated Radiology," stressed the necessity of binding and recementing the major segments—diagnostic roentgenology, therapeutic radiology and nuclear medicine—into an integrated whole. Certain changes are manifest as evidenced by the development of diagnostic roentgenology into diagnostic radiology with the embodiment of such procedures in nuclear medicine. The historic expansion of the official JOURNAL of our Society amply speaks for this need and clearly documents this chain of events. As we move into the space age, further contributions to the human kind may be realized from "space-born" radiations as have been gleaned from those which are "earthborn"—both natural and artificial. Steps in progress are frequently taken by those with necessarily detailed knowledge of various Disciplines but also with a perspective of their integrated applications. President Leucutia's Inaugural Address, published elsewhere in this issue of the JOURNAL, eloquently depicts the background of the past and the implications for the future of "Integrated Radiology."

The Scientific Session of the Society began immediately thereafter with the presentation on the first morning of nine papers on Special Procedures devoted to cardiovascular roentgenology and angiographic studies. The first of these explored various aspects of the significance of protein binding of contrast media in roentgen diagnosis. Cerebral angiography, angiography in determining the resectability of lung cancer, anomalous pulmonary venous return, pericardial effusion, aortic valvular disease, cardiac ventriculography, cardiac catheterization and intravascular nonsurgical grafting, and extra large field angiography were other methods and conditions discussed.

The programming of the scientific papers in the morning provided ample time for study of the scientific and technical ex-

hibits and attendance at the Instruction Courses. The Scientific Exhibits so capably arranged by the Committee under the Chairmanship of Dr. Charles O. Heilman, Fargo, North Dakota, are described in detail elsewhere in this issue of the JOURNAL.

On Tuesday evening the Annual Caldwell Lecture was delivered by Dr. Harold O. Peterson, Chairman, Department of Radiology of the University Hospitals and Professor of Radiology, University of Minnesota, Minneapolis, Minnesota. The title of his lecture was, "The Radiologist and the Special Procedures." Dr. Peterson was introduced by Dr. J. Paul Medelman, Director, Department of Radiology, St. Joseph's Hospital, St. Paul, Minnesota, and Clinical Associate Professor of Radiology, University of Minnesota, Minneapolis, Minnesota. Dr. Peterson's Lecture described the many facets of special diagnostic procedures performed by the radiologist and he emphasized that these procedures can often best be executed by the radiologist. The exceptionally large attendance and enthusiasm with which the audience received this Forty-first Annual Caldwell Lecture obviously expressed the importance of these procedures in present day diagnostic roentgenology and was a fine tribute to the outstanding abilities of Dr. Peterson. At the conclusion of the Lecture, President Leucutia presented to Dr. Peterson the Caldwell Medal, the highest award that our Society can offer for meritorious scientific achievement.

The Scientific Session was resumed on Wednesday morning with Dr. Ralph M. Caulk presiding. Most of the papers of this Session dealt with various aspects of diagnostic roentgenology with the last being a discussion of radiation hazards. It was emphasized that earlier predictions of biologic damage from radiation sources were unduly pessimistic and the radiologist was charged with the responsibility of realistically interpreting these various hazards.

The Scientific Session on Thursday morning with Dr. Clyde A. Stevenson presiding was also on various aspects of diagnostic roentgenology. One of the most interesting described the examination of the lower human colon by the use of a silicone foam. A soft mold is formed after its instillation which upon expulsion reveals imprints of mucosal abnormalities. In some instances cytologic examination can be carried out by recovering cells from the surface of the mold.

On Thursday afternoon a special instruction course, in the form of a Panel Discussion, on "Current Opinions from the American College of Radiology on Principles of Ethics, Economics and Facts and Figures" attracted a surprisingly large audience. Dr. Earl E. Barth moderated the Panel consisting of Drs. Bailey, Buchanan, Present and Wachowski. Dr. L. H. Garland, President of the American College of Radiology also participated in the timely discussion of these extremely important matters pertaining to radiologic practice which are of particular value to us younger radiologists.

On Thursday evening the Annual Banquet was held in the Casanova Room in a festive Caribbean atmosphere created by an excellent floor show of singing and interpretive dancing. The newly elected officers were announced with Dr. Earl E. Barth being the President-Elect of the Society. Awards were presented for those scientific exhibits judged to be outstanding.

On Friday morning with Dr. Robert C. Pendergrass presiding, ten papers on radiation therapy, one on the use of P^{32} in the evaluation of ocular neoplasms and one on newer trends in radiation therapy completed the program of the Scientific Sessions.

The Director of Instruction Courses, Dr. Harold O. Peterson, assisted by Dr. Donn G. Mosser, Associate Director, assembled an excellent array of courses, many of which dealt with the special procedures which Dr. Peterson discussed in the Caldwell Lecture. The fact that most were "sold-out" testifies to their popularity and value.

The number of technical exhibits was the

largest in the Society's history with complete utilization of the available space. These were assembled by Mr. Clifford L. Sherrat, Honorary Member, and Dr. James C. Cook, Manager of the Annual Meeting. A detailed list of the Technical Exhibits is published elsewhere in this issue of the JOURNAL.

The locale of the meeting in such a famous resort city as Miami Beach, along with the highly efficient and able efforts of the Committee on Local Arrangements, afforded delightful diversions for the ladies attending the meeting. On Monday, a Golf Widows' Boat Cruise to Fort Lauderdale and a tour of the tropical surroundings at Patricia Murphy's Candlelit Garden was capped by an excellent dinner. On Tuesday a tour to the Parrot Jungle with its exotically beautiful flowers and birds and a visit to the Seaquarium was coupled by lunch at the Key Biscayne Hotel. Wednesday found the ladies again cruising, this time toward the Villa Viscaya (an "Italian Palace in Miami") with its incomparable tapestries and furnishings, tropical gardens and statuary, many of which were imported from various castles in Europe, particularly Italy. The unusually good attendance on all of these trips was an obvious expression of the Committee's success. The Society is deeply appreciative of the diligent efforts of Mrs. Gerard Raap, Chairman, and Mrs. John S. Stewart, Co-Chairman and their charming Ladies Committee on Local Arrangements.

The Annual Golf Tournament, held at the La Gorce Country Club on Monday afternoon, was arranged by the Local Golf Committee under the chairmanship of Dr. Virgil H. Pieck. This course, one of the most scenic and beautiful on which this tournament has ever been held, afforded an enjoyable afternoon followed by the Golf Dinner at which the prizes were awarded.

To the Management and Staff of the Deauville Hotel the Society extends its sincere thanks for excellent service, a most pleasant atmosphere and the splendid manner in which all details of the meeting were carried out.

The Committee on Press Relations with Dr. David Kirsh as Chairman, and assisted by Mr. Otha W. Linton and Mr. David Pettengill from the American College of Radiology, ably handled press releases and public relations.

Dr. Gerard Raap deserves special commendation for his enthusiastic Chairmanship of the Committee on Local Arrangements. He truly embodied southern hospitality in its finest sense.

President Leucutia can feel pardonably proud for an eminently successful meeting which will be long remembered.

KENNETH L. KRABBENHOFT, M.D.

Harper Hospital
Detroit 1, Michigan



G. G. PALMIERI
1892-1961

PROFESSOR PALMIERI, who was born on February 6, 1892 in Bologna, Italy, received his medical degree in 1916 from the University of the same city. He was named Director of the Department of Medical Radiology of the University of Bologna in 1924, first in the capacity of Associated Professor and since 1939 as a full time Professor. In 1930 he also became Director of the L. Galvani Radium Institute of Bologna.

Professor Palmieri was Vice-President of the Società Italiana di Cancerologia in 1957 and of the Società Italiana di Radiobiologia

Medica in 1959. His many honors included the title of Accademico Benedettino dell'Accademia delle Scienze dell'Istituto di Bologna; honorary member of the Caroline-Leopold Academy of Halle and of the Medical Academy of the Republic of Colombia; honorary member of the Radiologic Societies of Germany, Austria, Czechoslovakia, Hungary, Spain, Mexico and Colombia; corresponding member of the Accademia di Scienze, Lettere e Arti di Modena and member of the Honorary Committee of Centre Antoine Béclère of Paris. He was an ardent supporter of the International Congress of Radiology and on two occasions headed the Italian delegation; in 1959 he was awarded the coveted Roentgenplakette in Monaco.

Professor Palmieri published more than 400 scientific papers pertaining to diagnostic and therapeutic radiology and was keenly interested in radiobiology. He gave freely of his time to lectures on many facets of practical radiology, took an enthusiastic part in scientific discussions, and was a devoted teacher with a gift of communicating thoughts of inspirational knowledge along with ideas of technical proficiency.

With the death of Professor Palmieri on August 16, 1961, the Italian Radiologic Society as well as world Radiology loses a brilliant scientist, an altruistic and affectionate physician, and a truly great man.

GIULIO TORI, M.D.

We regret to announce the death on September 4, 1961, at Baltimore, Maryland, of Dr. John W. Pierson, distinguished member and Past President of the American Roentgen Ray Society.

THE SCIENTIFIC EXHIBITS

THE SCIENTIFIC EXHIBITS of the Sixty-second Annual Meeting of the American Roentgen Ray Society held at the Deauville Hotel, Miami Beach, Florida, September 26–29, 1961, were of extremely high quality and most instructive. This year there was a considerable increase in the self-contained exhibits and this, with the beautiful decor of the Peacock Alley where they were displayed, immeasurably enhanced their attractiveness. The subjects of unusual technical achievements which were presented—many reflecting the importance of special procedures which were so vividly depicted by the Caldwell Lecturer of this meeting—furnished incontrovertible evidence of the extraordinarily rapid progress made in the science of radiology during the last few years. The Committee on Scientific Exhibits, under the very able chairmanship of Dr. Charles O. Heilman, Fargo, North Dakota, which spared no time or effort in making all the arrangements, has been amply compensated by the great interest shown by the members of the Society and their guests in these as well as in many other subjects of like documentary caliber. The Committee on Awards must have had a difficult task in selecting the exhibits most deserving of special merit. After careful and thoughtful consideration, one Silver Medal, one Bronze Medal, and eight Certificates of Merit were awarded.

Silver Medal

Lymphography; Lymphangio-Adenography. Manuel Viamonte, Jr., M.D., Manuel Soto, M.D., and Raymond E. Parks, M.D., Jackson Memorial Hospital and University of Miami School of Medicine, Miami, Florida.

The technique of the roentgenographic visualization of the lymph vessels and lymph nodes was illustrated in color transparencies. Two whole body roentgenograms and selected roentgenograms of conventional size illustrated the normal and abnormal findings in the clinical application of this technique.

The method is of definite value because: (1) it contributes to the detection and evaluation of the extension of lymph node metastasis; (2) it aids in the differential diagnosis of intra-abdominal and pelvic masses; (3) it assists in the evaluation of surgical, chemotherapeutic and radiotherapeutic management of malignant neoplasms; (4) it provides information as to the cause of obstructive edema, especially when combined with phlebography; and (5) it facilitates the diagnosis and treatment control of lymphomas.

The opacification of the lymph nodes is shown to better advantage on the 24 to 48 hour roentgenograms. The nodes remain radiopaque 6 to 8 weeks and in some cases as long as 6 months.

Delayed healing and infection of the wound are occasionally seen. Also, a miliary pattern may be observed in the lungs several hours after the injection, due to interstitial deposition of the ethiodol which is used as the opaque medium but this was found to be of no clinical significance.

It was concluded that lymphography represents a dynamic approach to the study of the anatomy, physiology and pathology of the lymphatic system with vast clinical and experimental potentialities.

Bronze Medal

Cerebral Angiography in Medical Practice; A Compendium of Clinical and Neuroroentgenologic Features. C. B. Holman, M.D., H. L. Baker, Jr., M.D., A. Uihlein, M.D., R. H. Miller, M.D., and A. H. Bulbulian, D.D.S., Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

In this exhibit the angiographic patterns of most of the intracranial tumefactive and vascular lesions were presented. The diagnostic features on the angiograms were readily apparent, because each was accompanied by a simplified explanatory diagram.

Information relating to the choice of patients, injection procedures and clinical complications was given *in extenso*.

CERTIFICATES OF MERIT

1. *The Detection of Upper Gastrointestinal Tract Pathology with High Kilovoltage Techniques.* Steven J. Figiel, M.D., Leo S. Figiel, M.D., Fred K. Wietersen, M.D., E. Lievois, M.D., D. K. Rush, M.D., and R. M. Balow, M.D., The Grace Hospital, Detroit Michigan.

High kilovoltage techniques and standard techniques were compared by presenting numerous cases. Roentgenographic studies of the surgical material with varying kilovoltages and Kodachromes of the surgical specimens were used to establish a final correlation between the roentgenologic and pathologic picture.

2. *Skeletal Abnormalities Associated with Gonadal Dysgenesis.* Nathaniel Finby, M.D., and Reginald MacGregor Archibald, M.D., Rockefeller Institute, New York, New York.

Gonadal dysgenesis is a genetic syndrome usually associated with an absent sex chromosome and a resultant XO pattern. Few of these patients have the classical "Turner's syndrome" but most do show skeletal abnormalities which are helpful in diagnosis. The abnormalities include dwarfism, slight retardation of skeletal maturation, metacarpal or carpal abnormalities with a positive "metacarpal sign," cubitus valgus and a "tibia-vara-like" deformity of the knees. The very young patient may show soft tissue edema and the older patient may show "osteoporosis."

The exhibit consisted of illustrative cases demonstrating these skeletal abnormalities.

3. *Juvenile Rheumatoid Arthritis.* William Martel, M.D., John F. Holt, M.D., and James T. Cassidy, M.D., University of Michigan, Ann Arbor, Michigan.

Certain roentgen manifestations of juvenile rheumatoid arthritis which differ from those observed in the adult type of the disease formed the theme of this exhibit.

Growth disturbances may be severe and periosteal new bone formation is frequent. Fractures and subluxations are often present. The atypical distribution of involved joints and the tendency toward cervical ankylosis are significant.

Other conditions requiring consideration in the differential diagnosis were also discussed.

4. *Bronchography: Diagnosis of Localized Peripheral Lesions.* William Molnar, M.D., Atis K. Freimanis, M.D., and William M. Blackwell, M.D., Ohio State University Hospital, Columbus, Ohio.

A method using an aerosol nebulizer for the introduction of topical anesthesia was described. The value of bronchography in the differential diagnosis of localized peripheral pulmonary lesions, not accessible to bronchoscopy, was illustrated by representative findings on bronchograms selected from a series of some 200 problem cases. The relatively greater extent of the bronchial divisions "seen" by bronchography as compared to bronchoscopy was emphasized.

5. *An In Vivo Dosimetry System for Clinical and Experimental Radiation Therapy.* Bernard Roswit, M.D., Stanley J. Malsky, M.A., M.Sc., Charles Amato, B.Sc., Cyprian B. Reid, B.Sc., Charles Spreckels, B.Sc., and Louis Maddalone, Mold Technologist, Veterans Administration Hospital, Bronx, New York.

The authors have designed and employed an *in vivo* human dosimetry system which has proved to be accurate and dependable and is relatively inexpensive. This system includes a detector, a reader, and a variety of tubes, needles, catheters and molds for *in vivo* applications.

The procedure was used in nearly every anatomic organ, tissue and space during clinical and experimental radiation therapy.

This exhibit described in detail the experience gained with the physical development and clinical use of the system.

6. *Tumors of the Small Intestine.* W. G. Sauer, M.D., W. H. Dearing, M.D., C. G. Moertel, M.D., M. B. Dockerty, M.D., C. A. Good, M.D., and A. H. Bulbulian,

D.D.S., Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Tumors of the small intestine are relatively uncommon and often present a diagnostic enigma to the physician. The authors have reviewed more than 700 tumors of the small intestine encountered at the Mayo Clinic in the 20 year period ending January 1, 1958. These tumors have been classified according to benignancy or malignancy, site or origin and relative frequency.

The commonest benign tumors in this group include leiomyoma, adenoma, lipoma and hemangioma; the commonest malignant neoplasms are carcinoid tumors, adenocarcinoma, malignant lymphoma and leiomyosarcoma.

This exhibit detailed the clinical features, laboratory and roentgenologic findings, gross and histologic characteristics, and the treatment recommended in each of these eight types of neoplasm. It also briefly outlined lesions that are seen much less frequently.

7. *Clinical Applications of Lymphangiography.* Sidney Wallace, M.D., Laird Jackson, M.D., Burton Schaffer, M.D., R. John Gould, M.D., Roy R. Greening, M.D., Simon Kramer, M.D., and Arthur Weiss, M.D., Jefferson Medical College Hospital, Philadelphia General Hospital, Philadelphia, Pennsylvania.

Lymphangiography by direct intralymphatic injection depicts the lymph vessels and lymph nodes of the extremities, inguinal, external and common iliac, and para-aortic areas, as well as of the axillary and supraclavicular areas and the thoracic duct.

In this exhibit the most useful clinical applications were demonstrated in detail.

8. *Fluid-Filled Loops in Intestinal Obstruction.* John L. Williams, M.D., and George A. Moller, M.D., The George F. Geisinger Memorial Hospital, The Foss Clinic, Danville, Pennsylvania.

In 6 per cent of 300 patients with intestinal obstruction, loops were filled with fluid but little or no gas. The incidence of gangrene is quite high in these fluid-filled obstructions and, therefore, the most dangerous cases are often the most difficult to diagnose. The correct roentgen diagnosis depends upon the recognition of the abnormal soft tissue densities caused by these fluid-filled loops. The abdomen is usually not distended and has no auscultatory signs.

The exhibit presented some unusual cases illustrating these points.

Other Exhibits

Other excellent exhibits were:

Radiology on Stamps. Stanley P. Bohrer, M.D., Massachusetts General Hospital, Boston, Massachusetts.

This exhibit consisted of first day covers, plate blocks, and other philatelic *objets d'art* documenting radiologic, nuclear, and atomic historic events. Correspondence from interested medical philatelists would be welcomed by the exhibitor.

The Value of the Admission Chest Film As an Aid in the Diagnosis of Extracardiac and Extrapulmonary Diseases in Children. Donald H. Altman, M.D., and Robert F. Conti, M.D., Variety Children's Hospital, Miami, Florida.

A group of 18 pediatric cases was discussed in which the admitting chest roentgenograms could be used to make a specific diagnosis, or strongly suggest the diagnosis, of extracardiac and extrapulmonary disease, later to be confirmed by additional studies.

The careful evaluation of all information available on the chest roentgenogram can frequently be a clue to obscure diseases in childhood even though the clinical information may be scant.

Dysgenesis of the Proximal Femur: Congenital Short Femur, Bowed Femur, and Coxa Vara. Harlan C. Amstutz, M.D., and Philip D. Wilson, Jr., M.D., Hospital for Special Surgery, Cornell Medical Center, New York, New York.

The development and variability of femoral neck-shaft valgus and version were presented. The roentgen characteristics of

coxa vara as a result of many acquired and congenital disturbances were illustrated. The roentgen features, pathogenesis, prognosis and treatment of three groups of seemingly related congenital ossification disturbances (congenital short femur with coxa vara, congenital bowed femur with coxa vara, and congenital coxa vara) were emphasized.

Azygography: Its Value in Mediastinal Metastases and Tumors. Arnold L. Bachman, M.D., Wolfgang Ackermann, M.D., and Kevin L. Macken, M.D., Columbia University, College of Physicians and Surgeons, New York, New York.

Roentgenographic demonstration of mediastinal metastases by the visualization of alterations and obstructions in the azygos venous system has proved to be of great importance in the determination of operability in carcinoma of the lung and esophagus.

In this exhibit were included the method of performing azygography, a description of the normal appearance and variations of the azygos veins, their appearance in nonneoplastic disease, the findings in carcinoma of the lung and esophagus, and in mediastinal tumors. Correlation with surgical and autopsy data was made.

The Mastoid. Joshua A. Becker, M.D., and Henry J. Woloshin, M.D., Temple University Medical Center, Philadelphia, Pennsylvania.

The resurgence of middle ear and mastoid surgery has brought new emphasis on mastoid roentgenography.

The authors attempted to establish a diagnostic regimen that will give the maximum amount of information, but which can be done with conventional roentgenographic equipment and without undue complexity. They obtained good preoperative correlation in 58 per cent of the cases with the surgical pathology findings. Further review yielded a 72 per cent correlation.

The exhibit gave a detailed account of the results.

The Post-Mortem Coronarogram. Donn J. Brascho, Captain, M.C., USA, Brooke General Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas.

The purpose of this exhibit was to demonstrate the results of a new and simple method for postmortem roentgenographic evaluation of the arterial supply of the human heart.

Improved Results in Treatment of Oral Carcinoma through Use of Precision Therapy with Custom Made Cones. S. Gordon Castigliano, M.D., and C. Jules Rominger, M.D., American Oncologic Hospital and Misericordia Hospital, Philadelphia, Pennsylvania.

The exhibitors presented improved results in the treatment of oral carcinoma during the last seventeen years using precision therapy with custom-made cones.

Protection can be assured to important uninvolved structures and adequate dosage can safely be delivered to well controlled volumes. Precision protection of adjacent tissues allows the performance of surgical procedures later with perfect healing.

Radioactive Phosphorus (P^{32}) for Diffuse Metastatic Bone Disease: The Third Decade of Use. Harold Chiat, M.D., and Perry Mandel, M.D., Nassau Hospital, Mineola, New York.

The technique of combined radioactive phosphorus (P^{32}) and testosterone for diffuse metastatic bone disease has had sufficient clinical evaluation to establish it as an important and rewarding therapeutic modality.

Representative cases were included in this exhibit with emphasis on the proper selection of patients, the technique of administration, the hazards, and the results.

Recent studies have clarified the involved physiologic mechanisms which suggest new areas worthy of further investigation.

Simple, Safe and Reliable Radiography of Infants. Donald B. Darling, M.D., Boston City Hospital, Boston, Massachusetts.

A method of obtaining the most routine studies in infants without radiation exposure to personnel was illustrated. The average gonad dose as measured during actual

exposure was indicated in each case. High speed screens, high speed films, 3 mm. Al filtration, double diaphragm collimation with full field illumination and 1/16 inch lead gonadal shields were employed.

The Solitary Dense Vertebral Body. John M. Dennis, M.D., University of Maryland, School of Medicine, Baltimore, Maryland.

Hodgkin's disease, Paget's disease and metastatic malignancy occasionally produce a solitary dense vertebral body. The etiology of this dense vertebral body can usually be determined roentgenographically from the bony architecture. These architectural changes produced by the three diseases were demonstrated.

Combined Roentgenologic and Gastroscopic Evaluation of Gastric Ulceration. Gerald D. Dodd, M.D., and Robert S. Nelson, M.D., University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

Combined roentgenologic and gastroscopic evaluation of gastric ulcers has proved highly accurate. A correlation of the significant differential points of each method of examination was illustrated by roentgenograms and color photographs made through the gastroscope. A statistical analysis of a series of 100 cases was presented.

Cranial Nerve Metastases in Tumors of the Head and Neck. Gerald D. Dodd, M.D., and Patrick A. Dolan, M.D., University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

Perineural and endoneural lymphatic vessels have proved to be important but neglected routes of spread in tumors of the head and neck. Existing therapeutic procedures can be modified to meet this contingency provided the clinician is aware of their actual or potential presence.

In approximately one-third of 37 proved cases at the M. D. Anderson Hospital, pretreatment recognition has proved feasible by plain film examination of the skull and facial bones by changes in the various transmittal canals and foramina of the major divisions of the cranial nerves. The roentgen anatomy of the most frequently involved nerves and the changes encountered with neural metastases were detailed.

Ectopic Ureterocele (Ectopic Ureter with Ureterocele). John P. Dorst, M.D., and Frederic N. Silverman, M.D., Departments of Radiology and Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio.

The most common type of ureterocele found in infants and children is an intravesical protrusion of the anterior aspect of a dilated ureter which passes between the mucosa and muscular coat of the bladder before it ends in the urethra. Termed an ectopic ureterocele, it differs from the better known simple ureterocele which characteristically occurs in the adult, in pathologic anatomy, size, severity of symptoms, prognosis, and therapy.

The pathologic anatomy and roentgenographic appearance of the two forms of ureterocele were contrasted, and the most common pitfalls in the diagnosis of the ectopic ureterocele were illustrated.

Flow Guided Catheterization and Nonsurgical Grafting: Two New Techniques for Cardiovascular Diagnosis and Treatment. Charles T. Dotter, M.D., and Kurt R. Straube, M.D., University of Oregon Medical School, Portland, Oregon.

The use of flexible tubing in place of ordinary cardiac catheters provides a simple means for downstream or flow guided catheterization of the pulmonary systemic arteries. The determination of man's pulmonary artery pressure requires neither skill nor fluoroscopy and can be done as a ward or office procedure.

Percutaneous spring guided arterial catheterization affords simple, experimentally established means for the nonsurgical insertion of silastic sleeve grafts into coronary, carotid, renal and peripheral arteries. If our "pipe dreams" are realized, this approach may assume considerable significance in the practice of medicine.

The exhibit demonstrated the two techniques.

An Evaluation of Roentgen Signs of Pan-

creatic Enlargement. William R. Eyler, M.D., Max D. Clark, M.D., and Roger L. Ryan, M.D., Henry Ford Hospital, Detroit, Michigan.

This exhibit consisted of selected roentgenograms from over 100 cases of pancreatic enlargement (*i.e.*, carcinoma, pancreatitis, pseudocysts and other less common causes) demonstrating the various roentgen signs. There was also a brief summary of some of the associated clinical findings.

The Colonic Polyp and Colonic Cancer. Detection, Significance and Roentgenographic Follow-Up of Colonic Polyps with the Use of High Kilovoltage Compression Technique. Steven J. Figiel, M.D., Leo S. Figiel, M.D., Fred K. Wietersen, M.D., Thomas Arminski, M.D., and D. W. McLean, M.D., The Grace Hospital, Detroit, Michigan.

The spot compression high kilovoltage method for detection of the colonic polyp was used to illustrate the development of colonic cancer from the colonic polypoid lesion.

Pertinent autopsy and histopathologic data were included. The authors presented comprehensive case material demonstrating their approach in determining the necessity for surgery when one or more colonic polyps are present.

Closed Circuit Television Tape and Direct Kinescopic Recording of the Fluoroscopic Image. Bertram R. Girdany, M.D., and Edwin S. Gaither, M.D., Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania.

The individual components that make up a closed circuit television fluoroscopic system and tape recorder were explained in words and diagrams. The advantages of television tape recording were listed. Table top radiation dosages during actual recording were tabulated. A live kinescopic film was shown.

The Pineal Laminagram: Visualization of the Faintly Calcified Pineal Gland. John A. Goree, M.D., Karl K. Wallace, Jr., M.D., and Richard L. Bean, M.D., Department of Radiology, Duke University Medical Center, Durham, North Carolina.

The small pineal calcification is usually clearly visible on a lateral roentgenogram of the skull but is often obscured in all anteroposterior and posteroanterior projections, including stereoscopic films. Laminagraphy will demonstrate pineal calcification in many such instances and make localization of this structure possible. A simple technique and illustrative cases were presented.

Roentgen Findings in Diseases with Abnormal Calcifications. Theodore F. Hilbish, M.D., and Frederic C. Bartter, M.D., National Institute of Health, Clinical Center, Bethesda, Maryland.

This exhibit presented the roentgen findings of diseases associated with abnormal calcium deposition including such conditions as metastatic calcification, calcinosis, dystrophic calcification, heterotopic bone formation, vascular calcification and stone formation. The exhibit was intended to portray the interesting and, at times, unusual calcium depositions observed within the body tissues. Brief comments concerning the diagnosis were included in the exhibit.

Intercalated Segmental Pulmonary Arteriography. J. C. Hirschman, M.D., Manuel Viamonte, Jr., M.D., R. J. Boucek, M.D., and Raymond E. Parks, M.D., Jackson Memorial Hospital and University of Miami School of Medicine, Miami, Florida.

This method of angiography, which makes use of electronically programmed injection of the opaque medium and the roentgen ray exposure, was applied to the study of pulmonary vascular physiology and pathology. Experimental work in dogs and humans has demonstrated the presence of pulmonary vasomotor responses and some more permanent pathologic changes in various disease states.

Venography in Thrombophlebitis of the Lower Extremity: A Useful Techniuqe in Diagnosis and in the Evaluation of Thrombolytic Agents. Richard A. Kramer, M.D., Sydney P. Hecker, M.D., and John F.

Weigen, M.D., Palo Alto Medical Clinic (Departments of Radiology and Internal Medicine), Palo Alto, California.

Venography of the lower extremity is useful both in establishing the diagnosis of thrombophlebitis and in evaluating the efficacy of treatment. Many conditions can simulate the clinical appearance of thrombophlebitis, and in equivocal cases venography can be a valuable diagnostic adjunct to the usual clinical studies. Venography also offers an objective way of comparing the efficacy of various thrombolytic agents.

Plasmin is currently being evaluated in the treatment of stroke, coronary occlusion and peripheral arterial occlusion in addition to thrombophlebitis. Angiographic techniques will be invaluable in these studies.

This exhibit illustrated valuable points pertaining to these studies.

Polydirectional Body-Section Radiography with the Polytome. J. T. Littleton, M.D., C. L. Rumbaugh, M.D., and F. S. Winter, M.D., The Guthrie Clinic and Robert Packer Hospital, Sayre, Pennsylvania.

This exhibit served to introduce the use of polydirectional body-section roentgenography in all of its phases through the use of the Polytome. This is the first unit of its type to be employed in the United States, although it has become a fairly common method in Europe. It is the feeling of the authors that this instrument offers a diagnostic advantage which has heretofore not been fully appreciated in the United States.

Contrast Roentgenography of the Larynx. Jose T. Medina, M.D., William B. Seaman, M.D., Ira Kanter, M.D., P. Carbajal, M.D., and D. Baker, M.D., Columbia-Presbyterian Medical Center, New York, New York.

The technique of the roentgen examination of the larynx and hypopharynx by the instillation of oily dionosil after local anesthesia was described. The resultant coating of the mucosa produces a double contrast image of the larynx, hypopharynx and upper trachea with anteroposterior and lateral films exposed (1) during quiet breathing through the nose with the mouth closed, (2) during phonation of the vowel Eeeee, (3) while performing the true Valsalva maneuver, and (4) while performing a modified Valsalva maneuver by blowing through the closed lips.

Examples of the normal anatomy, anatomic variants, and various pathologic states have been selected for exhibition from a total clinical materal of almost 200 patients.

Intravenous Abdominal Arteriography. William T. Meszaros, M.D., John B. Graham, M.D., Howard C. Burkhead, M.D., Myles P. Cunningham, M.D., George C. Sutton, M.D., and Brown Brooks, M.D., Cook County Hospital, Evanston Hospital, and Northwestern University Medical School, Chicago and Evanston, Illinois.

Intravenous arteriography is a relatively new method of visualizing the abdominal aorta and its branches. Roentgenologic examination of the aorta is performed following intravenous injection of contrast material. The value and limitations of this procedure were shown on films illustrating various types of vascular abnormalities.

Detection of Regional Lung Function and Early Carcinoma by Fluorodensimetry. Charles P. Oderr, M.D., Veterans Administration Hospital, New Orleans, Louisiana.

Simultaneous electronic recording of fluoroscopic density during breathing maneuvers in two similar areas makes it possible to detect a relative impairment of function in one. The record made reveals the change in density with quiet, deep and fast breathing as well as during cough. The loss of amplitude in expansion and contraction of a given lobe is probably earlier evidence of endobronchial disease, such as carcinoma, than either atelectasis or emphysema.

These pertinent points were demonstrated in the exhibit.

The Problem of the Overexposed Film: Practical Methods of Film Reduction. An-

drew K. Poznanski, M.D., C.M., Henry Ford Hospital, Detroit, Michigan.

Many of the well known photographic reducers are not ideally suited for the relatively high density, high contrast, double emulsion roentgen-ray film. A search was made for a reducer that would be effective on roentgen-ray film and be simple to use. A copper sulphate reducer was found to be simple to use, stable when stored, not highly toxic and its components are readily available.

In this exhibit the procedure was described in detail and other methods of film reduction, including removal of one emulsion and the use of the logEtron, were compared.

Parosteal Osteoidsarcoma. Klaus Ranniger, M.D., Department of Radiology, University of Chicago, Chicago, Illinois.

The roentgenologic appearance and the clinical behavior of parosteal osteoidsarcoma (juxtacortical osteosarcoma) are distinctly different from other bone sarcomas, particularly from the usual type of osteosarcoma. Eleven cases with follow-up examinations were presented which demonstrated the typical roentgenologic features and the slow progression of this variant of osteosarcoma.

Shelf Tumors and Their Differential Diagnosis. Julian O. Salik, M.D., Sinai Hospital of Baltimore, Inc., Baltimore, Maryland.

Pathologic changes in the recto-uterine or recto-vesical excavation may be caused by benign or malignant tumors or may be of inflammatory origin. The roentgen appearance and differential diagnosis in male and female were illustrated by representative cases.

Case of the Day. Stefan C. Schatzki, M.D., Walter Reed General Hospital, Washington, D. C.

A "Case of the Day" for interpretation by those attending the meeting was presented. On the subsequent day the pathologic findings were given and discussion of the previous day's films was held.

This exhibit brought attention to a potential method of teaching that has proved successful in several Departments of Radiology.

Lesions Presenting in Right Cardiophrenic Angle. Hildegarde Schorsch, M.D., Edward A. Piszczek, M.D., M.P.H., and Ki Eun Chung, M.D., Cook County Hospital, Stritch School of Medicine, Loyola University, The Suburban Tuberculosis Sanitarium District, Chicago, Illinois.

The differential diagnosis of lesions which project into the right cardiophrenic angle in the plain chest roentgenogram was discussed.

These lesions, based on etiology, were classified into 7 groups: (1) upper gastrointestinal; (2) diaphragmatic hernia; (3) pulmonary; (4) cardiovascular; (5) pleural; (6) intrathoracic tumors; and (7) miscellaneous.

Representative cases were illustrated.

Estimation of Experimental Coronary Hemodynamics by Coronary Cine-Arteriography. William H. Sewell, M.D., Veterans Administration Hospital, Oteen, North Carolina.

Coronary cinearteriograms were taken at 30 frames per second on 35 mm. Plus-X film by injecting 90 per cent hypaque into the sinus of Valsalva of dogs. Both the diameter and rate of movement of the medium in the anterior descending artery were compared with the circumflex, before and after various degrees of surgical construction of the anterior descending branch. After the standard deviation of the method was determined, it was possible to tell whether a surgical constriction had significantly reduced the relative flow in the anterior descending artery and to estimate the degree of change.

The exhibit demonstrated the results obtained in detail.

The Differential Diagnosis of Vertebral Body Compression. William C. Strittmatter, M.D., and Barry Q. Walker, M.D., Cleveland Clinic Foundation, Cleveland, Ohio.

In this exhibit some of the lesions that cause compression of vertebral bodies were

presented. They were divided into six main groups (1) traumatic, (2) infectious, (3) neoplastic, (4) metabolic, (5) vascular; and (6) systemic disorders of unknown etiology.

Representative examples of each group were included in an attempt to aid the radiologist in arriving at a correct diagnosis.

Roentgenographic Examination of the Vocal Cords. Sol M. Unger, M.D., Harold G. Jacobson, M.D., George A. Meyer, M.D., H. Kolson, M.D., and Maxwell H. Poppel, M.D., Veterans Administration Hospital, Bronx, New York.

Roentgenographic examination of the larynx can easily be carried out by means of laminagraphy, or by conventional spot films during fluoroscopy. Vocal cord paralysis secondary to recurrent laryngeal nerve paralysis and vocal cord irregularity due to carcinoma of the larynx can be differentiated and this was demonstrated by the exhibitors.

The normal and abnormal larynx can also be adequately visualized on conventional roentgenograms. The anatomy of the larynx was thoroughly and clearly discussed.

A Second Look Is Worth 1,000 X-Rays: Tuberculosis Program. U. S. Department of Health, Education, and Welfare, Public Health Service, Washington, D. C.

The case for dual reading of roentgenograms in tuberculosis case finding was presented. Facilities were available at the exhibit to allow physicians to check their interpretations of sample films against those of experts. In an accompanying pamphlet studies were cited showing that dual reading increases the yield by 10 per cent or more thereby reducing radiation exposure.

The Roentgenographic Determination of Pulmonary Hypertension in Mitral Stenosis. Manuel Viamonte, Jr., M.D., Frank Barreras, M.D., and Raymond E. Parks, M.D., Jackson Memorial Hospital and University of Miami School of Medicine, Miami, Florida.

In this exhibit the criteria used for predicting the mean pulmonary artery pressure in patients with mitral stenosis were presented. Examples of cases with absent, minimal, moderate and severe pulmonary arterial hypertension were shown. Other pulmonary findings in mitral stenosis were also demonstrated. Postoperative studies should be performed 6 months to 1 year after surgical intervention.

THE TECHNICAL EXHIBITS

The Technical Exhibits of the Sixty-second Annual Meeting of the American Roentgen Ray Society, held in Miami Beach, Florida, September 26–29, 1961 were the largest and most attractive in the Society's history. The matchless convention engineering concept embodied in the Deauville Hotel, the spacious exhibit halls, Napoleon Room No. 1 and 2, and their location in the immediate vicinity of the activities of the Scientific Assembly were pleasant features equally welcomed by the Exhibitors and the many members and guests of the Society who visited them. The displays, which were artistically arranged and unprecedently beautiful, evoked the greatest admiration and thereby contributed notably to the over-all success of the meeting.

The untiring efforts of Mr. Clifford L. Sherratt, Honorary Member, and Dr. James C. Cook, Manager of the Annual Meeting were again amply rewarded by the fact that the ultramodern facilities of the Deauville Hotel were utilized to fullest extent. The Society extends its most sincere thanks to the many exhibitors for their participation at this Sixty-second Annual Meeting and regrets that, despite the increased space, a few of the applicants could not be accommodated.

The following are the firms which took part in the Technical Exhibits:

Abbott Laboratories, North Chicago,

Illinois; Ansco Division, General Aniline & Film Corporation, Binghamton, New York; Atomic Energy of Canada Limited, Ottawa, Canada; Automatic Seriograph Corporation, College Park, Maryland; Barnes-Hind Barium Products Company, Sunnyvale, California; Bar-Ray Products, Inc., Brooklyn, New York; Bell-Craig, Inc., New York, New York; Carr Corporation, Santa Monica, California; Cordis Corporation, Miami, Florida; Lester A. Dine Company, Woodside, New York; Dunlee Corporation, Bellwood, Illinois; E. I. du Pont de Nemours & Company, Inc., Wilmington, Delaware; Eastman Kodak Company, Rochester, New York; Encyclopaedia Britannica, Miami, Florida; Eureka X-Ray Tube Corporation, Chicago, Illinois; Oscar Fisher Company, Inc., Newburgh, New York; E. Fougera & Company, Inc., Hicksville, Long Island, New York; Franklin X-Ray Corporation, Philadelphia, Pennsylvania; General Electric Company, Milwaukee, Wisconsin; Gordon Consultants, New York, New York; Great Books of the Western World, Baltimore, Maryland; Grune & Stratton, Inc., New York, New York; Halsey X-Ray Products, Inc., Brooklyn, New York; Paul B. Hoeber, Inc., New York, New York; Hospital Microfilming Company, Pearl River, New York; Howdon Videx Products Corporation, Mount Vernon, New York; Philip A. Hunt Company, Palisades Park, New Jersey; Ilford, Inc., New York, New York; Keleket X-Ray Corporation, Waltham, Massachusetts; Leishman X-Ray Engineering Corporation, Los Angeles, California; Liebel-Flarsheim Company, Cincinnati, Ohio; Low X-Ray Corporation, New York, New York; Machlett Laboratories, Inc., Springdale, Connecticut; Mallinckrodt Chemical Works, St. Louis, Missouri; Mattern X-Ray Division—Land Air, Inc., Chicago, Illinois; Micro X-Ray Recorder, Inc., Chicago, Illinois; North American Philips Company, Inc., New York, New York; Nuclear-Chicago Corporation, Des Plaines, Illinois; Pako Corporation, Minneapolis, Minnesota; Pennsylvania X-Ray Corporation, Glenside, Pennsylvania; Physicians' Technical Equipment Company, Milwaukee, Wisconsin; Picker X-Ray Corporation, White Plains, New York; Profexray, Inc., Maywood, Illinois; W. B. Saunders Company, Philadelphia, Pennsylvania; Schick X-Ray Company, Inc., Chicago, Illinois; Frank Scholz X-Ray Corporation, Boston, Massachusetts; Siemens New York, Inc., New York, New York; E. R. Squibb & Sons, New York, New York; Standard X-Ray Company, Chicago, Illinois; Charles C Thomas, Publisher, Springfield, Illinois; Thuresson-Angrabright-Bennett, Inc., Skokie, Illinois; United States Radium Corporation, Morristown, New Jersey; Westinghouse Electric Corporation, Pittsburgh, Pennsylvania; Winthrop Laboratories, New York, New York; X-Ray Solutions Services, Detroit, Michigan; Year Book Medical Publishers, Inc., Chicago, Illinois.

NEWS ITEMS

AMERICAN ROENTGEN RAY SOCIETY ELECTS OFFICERS

At the Sixty-second Annual Meeting of the American Roentgen Ray Society held at the Deauville Hotel in Miami Beach, Florida, September 26–29, 1961, the following officers were elected: President, Dr. Traian Leucutia; President-Elect, Dr. Earl E. Barth; First Vice-President, Dr. Ralph M. Caulk; Second Vice-President, Dr. Richard Schatzki; Secretary, Dr. C. Allen Good; Treasurer, Dr. Stephen W. Brown. Dr. Robert C. Pendergrass is the newly elected Chairman of the Executive Council.

The Sixty-third Annual Meeting of the Society will be held October 2–5, 1962, in Washington, D.C.

AMERICAN COLLEGE OF RADIOLOGY CONFERS HONORARY MEMBERSHIP

The American College of Radiology held a special convocation in São Paulo on Wednesday, September 6, 1961 to confer honorary membership on the following: Dr. Luis Arrieta-Sanchez, Editor of *Radiología* of Panamá; Dr. Nicola C. Caminha, President of the Brazil College of Radiology, Rio de Janeiro, Brazil; and Dr. Antonio Pinto-Vieira, Director of the Institute of Cancer, Rio de Janeiro, Brazil.

The convocation was presided over by Dr. Philip J. Hodes. Dr. E. P. Pendergrass acted as Chairman of the Board of Chancellors; Dr. Ross Golden as Sergeant of Arms. Dr. J. A. del Regato read the citations of the new members in Portuguese.

FOURTEENTH ANNUAL MIDWINTER RADIOLOGICAL CONFERENCE

The Fourteenth Annual Midwinter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Biltmore Hotel, Los Angeles, California, on Saturday and Sunday, February 3 and 4, 1962.

An outstanding program of pertinent interest has been arranged and the guest speakers will be Doctor David Sutton, Saint Mary's Hospital, London, England; Doctor Scott Dunbar, Montreal Children's Hospital, Montreal, Canada; Doctor Richard Marshak, Mt. Sinai Hospital, New York, New York; Doctor Gilbert Fletcher, M. D. Anderson Hospital, Houston, Texas; and Doctor Henry Kaplan, Stanford Medical Center, Stanford, California.

The conference fee of $25.00 includes two luncheon meetings featuring questions and answers. A banquet ($7.50 per plate) preceded by cocktails will be held Saturday evening at the Biltmore Bowl. Reservations may be made through: V. G. Mikity, M.D., 2010 Wilshire Boulevard, Los Angeles 57, California.

Courtesy cards will be available to residents in radiology and Radiologists in the Armed Forces by advance registration, with reduced tariff for luncheons and banquet. Hotel reservations should be made through the Convention Manager, Biltmore Hotel, Los Angeles, California.

UNIVERSITY OF MINNESOTA ANNOUNCES CONTINUATION COURSE

The University of Minnesota announces a Continuation Course in Urologic Radiology for Radiologists, Nov. 6–10, 1961.

Guest participants will include Doctors Guido Currarino, New York; Arthur T. Evans, Cincinnati; John A. Evans, New York; Carl L. Gillies, Iowa City; James O. Hoppe, Rensselaer, New York; John A. Hutch, San Francisco; Harry Z. Mellins, Brooklyn; Olle Olsson, Sweden; Eugene F. Poutasse, Cleveland; Vincent Vermooten, Fort Sam Houston, Texas; and Keith Waterhouse, Brooklyn.

For information write: Director, Center for Continuation Study, University of Minnesota, Minneapolis, Minn.

BOOKS RECEIVED

THE FUNDAMENTALS OF X-RAY AND RADIUM PHYSICS. Third edition. By Joseph Selman, M.D., Clinical Assistant Professor of Radiology, University of Texas, Southwestern Medical School; Director, School for X-ray Technicians, Tyler Junior College; Director, Radiology Department, Medical Center Hospital; Attending Staff in Radiology, Mother Frances Hospital; Consultant in Radiology, East Texas Tuberculosis Hospital, Tyler, Texas. Cloth. Price, $8.50. Pp. 364, with illustrations and tables. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

RESPIRATION IN HEALTH AND DISEASE. By R. M. Cherniack, M.D., M.Sc., F.R.C.P. (C.), Assistant Professor of Medicine, University of Manitoba School of Medicine; Director, Respiratory Division, Clinical Investigation Unit, and Assistant Physician, Winnipeg General Hospital; Consultant in Respiratory Diseases to Children's Hospital and Municipal Hospitals, Winnipeg, Canada; and L. Cherniack, M.D., B.Sc., M.R.C.P. (Lond.), F.R.C.P. (C.), F.A.C.P., Assistant Professor of Medicine, University of Manitoba School of Medicine; Associate Physician, Winnipeg General Hospital; Physician, Division of Medicine, Winnipeg Clinic, Winnipeg, Canada. Cloth. Pp. 403, with 92 illustrations. W. B. Saunders Company, 218 West Washington Square, Philadelphia, 1961.

ADVANCES IN OTO-RHINO-LARYNGOLOGY. Vol. VIII. Edited by Prof. Dr. L. Rüedi, Zürich, Switzerland. Cloth Price, $13.00. Pp. 431, with numerous illustrations. S. Karger, Basel, Switzerland. In the U. S. A. and Canada, Albert J. Phiebig, P. O. Box 352, White Plains, N. Y., 1961.

ADVANCES IN TUBERCULOSIS RESEARCH. Vol. II. Edited by Dr. Hubert Bloch, Pittsburgh, Pennsylvania. Cloth. Price, $18.00. Pp. 282, with illustrations. S. Karger, Basel, Switzerland. In the U. S. A. and Canada, Albert J. Phiebig, P. O. Box 352, White Plains, N. Y., 1961.

RECONSTRUCTION SURGERY AND TRAUMATOLOGY. Edited by E. L. Compere, Chicago, Illinois. Cloth. Price, $11.00. Pp. 139, with many illustrations. S. Karger, Basel, Switzerland. In the U. S. A. and Canada, Albert J. Phiebig, P. O. Box 352, White Plains, N. Y., 1961.

PUBLIC HEALTH PAPERS. No. 6. IONIZING RADIATION AND HEALTH. By Bo Lindell, Institute of Radiophysics, Stockholm, Sweden; and R. Lowry Dobson, Chief Medical Officer, Radiation and Isotopes, World Health Organization, Geneva, Switzerland. Paper. Price, $1.00 Pp. 81, with many tables. World Health Organization, Geneva, Switzerland. In the U. S. A., Columbia University Press, International Documents Service, 2960 Broadway, New York, N. Y., 1961.

PUBLIC HEALTH PAPERS. No. 9. TEACHING OF PSYCHIATRY AND MENTAL HEALTH. Contributors: M. Bleuler, O. V. Kerbikov, E. E. Krapf, T. A. Lambo, S. Lebovici, Tsung-yi Lin, I. Matte-Blanco, M. Ostow, T. F. Rodger, J. Stoetzel, and E. S. Turrell. Paper. Price, $2.00. Pp. 186, with tables. World Health Organization, Geneva, Switzerland. In the U. S. A., Columbia University Press, International Documents Service, 2960 Broadway, New York, N. Y., 1961.

RADIOGRAPHIC ANATOMY OF THE HUMAN SKELETON; A HANDBOOK FOR RADIOGRAPHERS. By W. H. Johnson, F.S.R., Lecturer in Radiographic Anatomy, 1940–1956, for the Society of Radiographers Membership Examination at the Ilford Department of Radiography and Medical Photography, Tavistock House, London; and J. A. Kennedy, M.B., M.R.C.S., D.M.R., D.M.R.D., Lecturer in Radiological Anatomy, King's College, University of London, Senior Radiologist, St. Helier Hospital, Carshalton, England. Cloth. Price, $10.00. Pp. 280, with 233 illustrations. Williams & Wilkins Company, 428 East Preston Street, Baltimore, 1961.

THE YEAR BOOK OF CANCER, 1960–1961. Compiled and edited by Randolph Lee Clark, Jr., B.S., M.D., M.Sc. (Surgery), D.Sc. (Hon.), Director and Surgeon-in-Chief, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Surgery, The University of Texas Postgraduate School of Medicine; Clinical Professor of Surgery, Baylor University College of Medicine; Chairman, Committee on Cancer, American College of Surgeons; F.A.C.S.; and Russell W. Cumley, B.A., M.A., Ph.D., Director of Publications, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Medical Journalism, The University of Texas, Postgraduate School of Medicine; Executive Editor, Medical Arts Publishing Foundation, Houston, Texas. Cloth. Price, $8.50. Pp. 539, with 189 illustrations. Year Book Medical Publishers, Inc., 200 East Illinois Street, Chicago, 1961.

BRITISH COLUMBIA CANCER INSTITUTE, VANCOUVER; FIVE YEAR RESULTS OF TREATMENT 1946–1954 WITH A SYNOPSIS OF TREATMENT POLICY 1961. By A. Maxwell Evans, M.D., C. M., D.M.R.E., Director, British Columbia Cancer Institute, Clinical Assistant Professor, Department of Surgery, University of British Columbia, Cloth. Pp. 269. British Columbia Cancer Institute, 2656 Heather Street, Vancouver 9, B.C., 1961.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Steven, J. L. Some pitfalls in the angiographic diagnosis of intracranial tumour pathology. *Clin. Radiol.*, July, 1961, *12*, 194–198. (From: West of Scotland Neurosurgical Unit, Killearn Hospital, Glasgow, Scotland.)

Angiographic diagnosis of the nature of a tumor is now being readily accepted by neurologists and neurosurgeons, throwing a correspondingly greater burden on the radiologist. The author gives 3 case histories in which the angiographic appearances were unusual.

Case 1. A diagnosis of meningioma was made on the basis of the angiographic findings. Complete occlusion of the left internal carotid artery at its origin was demonstrated, and there were two areas of abnormal vasculature in the superficial left frontoparietal region. At craniotomy no tumor was found. The misleading appearance may have been due to some form of anastomotic circulation via the superficial temporal artery and the middle meningeal artery, but this is mere speculation.

Case 2. Right common carotid angiography showed mid-line vessels displaced to the left, and several small wooly opacities of different sizes appeared in the late arterial and capillary phases. These had cleared in the venous phase. A diagnosis of multiple tumors was suggested. At postmortem examination there were multiple hemorrhagic infarcts corresponding in position to the opacities seen on the roentgenograms. Presumably the opacities were due to contrast medium circulating through numerous dilated capillaries adjacent to the ischemic zones.

Case 3. A left carotid angiogram revealed a small knot of vessels in the posterior temporal region with an early filling vein draining the area. This was interpreted as a small arteriovenous malformation. Five weeks later a repeat left angiogram revealed a marked shift of mid-line vessels to the right, elevation of the middle cerebral group of vessels, and a large area of poorly defined tumor vessels. The patient expired seven days later. A postmortem examination was not made, but the roentgenographic appearance indicated a rapidly growing glioblastoma.—*Samuel G. Henderson, M.D.*

Tori, G., and Garusi, G. F. Left carotid-jugular arteriovenous fistula; angiocardiographic study before and after surgical operation. *Radiol. clin.*, 1961, *30*, 76–85. (Address: G. Tori, Institute of Radiology and Radium Institute of the University, Bologna, Italy.)

This is a case report of a five year old boy with a congenital left carotid-jugular arteriovenous fistula. This had caused a large left to right extracardiac shunt and had resulted in cardiomegaly and heart failure.

On angiocardiography the left common carotid was dilated to three times normal size and appeared to be twisted. There were two large shunts (0.5 cm.) between the left common carotid and the external jugular vein, one near the angle of the jaw and the other 4 cm. lower. The left innominate vein was markedly dilated and tortuous. At surgery, the abnormal shunts were removed and there was immediate improvement in the patient's symptoms.

Three years after surgery a chest film disclosed marked reduction in the size of the heart. An angiocardiogram showed that the left common carotid was still considerably enlarged but no shunt was present.—*J. L. Williams, M.D.*

Tindall, George T., and Cupp, Horace B., Jr. Vertebral arteriography by retrograde injection of the right common carotid artery. *Radiology*, May, 1961, *67*, 742–747. (Address: G. T. Tindall, Department of Surgery, Duke University Medical Center, Durham, N. C.)

The authors describe a simple, percutaneous method for obtaining vertebral arteriograms during the course of carotid arteriography. The basic feature of this method is that a thin-wall 17 gauge needle is inserted into the right common carotid artery, below the carotid bifurcation, with the point directed toward the heart. An injection of 20 cc. of 50 per cent hypaque is made manually in a retrograde direction with compression on the common carotid artery above the needle and on the ipsilateral brachial artery. Exposures are made at the completion of the injection, producing diagnostic vertebral arteriograms in the majority of cases. A slower injection of 10 cc. of 50 per cent hypaque, without vessel compression, allows direct right carotid arteriography.

Critical analysis of 125 injections in a group of 60 patients revealed diagnostic vertebral angiograms in 42 patients, or 70 per cent. The majority of failures was due to improper timing or incomplete compression of the distal carotid artery. This latter observation prompts the recommendation that the same concentration of contrast medium used for carotid arteriograms should be used for the retrograde vertebral arteriograms. Retrograde injections were made into the left common carotid artery in 6 patients without visualization of either the left vertebral or subclavian arteries.

The two chief advantages of the retrograde method are that it avoids direct puncture of the vertebral artery and can be accomplished under local anesthesia. It is especially worthy of consideration in patients with thrombosis of the internal carotid artery since it avoids the risk of threading

the tip of the needle into the involved portion of the vessel. Although the one "blind spot" in this technique is the failure to visualize the left vertebral artery, a complete survey of the intracranial arterial circulation can be accomplished in one session, through bilateral carotid artery punctures.—*Edward B. Best, M.D.*

Ostrowski, A. Z., Hardy, W. G., Lindner, D. W., Thomas, L. M., and Gurdjian, E. S. Retrograde brachial vertebral-basilar angiography; an analysis of angiographic visualization of the vertebral-basilar system and branches. *A.M.A. Arch. Neurol.*, 1961, *4*, 608–616. (Address: E. S. Gurdjian, Wayne State University, 1401 Rivard St., Detroit 7, Mich.)

Extracranial vascular occlusive lesions in the stroke syndrome were investigated in 90 patients by the effective and safe method of retrograde brachial angiography. In the earlier cases, open arteriotomy and general anesthesia was practiced; later, percutaneous technique with a 17 gauge spinal needle in each brachial artery was successful. About 20 cc. of 50 per cent hypaque was used for each of the 4 to 6 manual injections required to obtain angiograms in varying projections. (It is of note that "as much as 300 ml." of the opaque medium was employed in some cases!) No important complications occurred.

The technique produced visualization of the right carotid in 75 cases; of the left carotid in 3 cases. Opacification of the left carotid occurred only with injection of the right brachial and success seemed dependent on an anomalous origin from a common innominate. Both vertebrals (when patent) were opacified in all cases. In only a third of the carotids shown could the origin of the vessel be seen; the origin of the vertebrals was seen in the majority. In over half of the group, the origin of the posterior inferior cerebellar artery was shown. Evaluation of the basilar arteries was often permitted by this method.

Artifact or anomaly may be suspected when a portion of the vertebral-basilar system is not opacified, but in the majority this sign indicates disease. Left and right vertebrals are rarely of the same caliber and nonfilling of the intracranial portion of the vertebral artery was usually interpreted as artifact if it was on the side of the smaller vertebral and if the basilar artery filled from the opposite larger vertebral. Among those suspected of vascular occlusive disease the procedure strongly supported this diagnosis (*i.e.*, 77 per cent showed atheromatous abnormalities.)

Finer points of technique are not described but references are supplied and should be consulted. When occlusive disease of the vertebral-basilar system is suspected this would seem to be the diagnostic procedure of choice because of its safety and reliable graphic result. The hemorrhage and pneumothorax which may attend the percutaneous subclavian approach are avoided. The important site, the origin of the vessel, is usually demonstrated as it often is not in a percutaneous vertebral artery puncture. One should not anticipate opacification of the left carotid by this method and poor visualization of the origin of the right carotid is a deficiency shared by most techniques. The role played by hydrodynamics to prevent opacification of portions of the system and thus mimic structural occlusion is the *bête noire* of angiography of the posterior fossa and will help to keep medicine an art.—*Jack Reynolds, M.D.*

Oller, Jose L. Garcia, Nelson, N., Espenan, P., Fernandez, W., Mathirne, C., and Haydel, W. Angiography by brachiovertebral and temporal arterial catheter. *South. M. J.*, Apr., 1961, *54*, 345–349. (From: The Department of Neurosurgery Mercy Hospital, and the Independent Neurosurgery Service, Charity Hospital, New Orleans, La.)

The authors summarize their results in angiography of the cerebral vessels by direct arterial catheterization. Brachial angiography makes possible routine studies of the vertebral circulation with freedom from spasm and direct injury plus visualization of the carotid artery. The authors also utilized catheterization of the temporal arteries and occasionally they combined the procedures by using the right brachial and left temporal arteries in one examination. This combined procedure produced an excellent one stage cerebral angiogram.

They conclude that catheterization of the brachial artery is safe and reliable for routine vertebral angiography, as is temporal catheterization for carotid angiography, with the latter also being an excellent technique for pediatric patients. They found that critically ill patients with head injuries and subarachnoid hemorrhage are accurately and safely studied with catheterization techniques. Also, vertebral angiography gave essential diagnostic information in one-third of the cases of brain tumors studied.—*Richard L. Jontz, M.D.*

Lamb, John, and Morris, Leon. The carotid-basilar artery; a report and discussion of five cases. *Clin. Radiol.*, July, 1961, *12*, 179–186. (From: X-ray Department, Brook Hospital, Shooters Hill Road, London, S.E. 18, England.)

An anomalous vessel joining the carotid and basilar arteries has been known to anatomists since it was first described by Quain in 1844. The first case diagnosed during life by angiography was described by Sutton in 1950.

The authors give 5 case histories in which this

anomalous vessel was found by arteriographic examination. They state that their experience and a study of the literature show that, in almost all cases, the anomaly is found incidentally during the course of routine angiography. Of their 5 patients, the first had a metastatic cerebral tumor, the second was angiographically normal apart from the anomalous vessel, the third had an intracerebral hematoma associated with a hemisphere angioma, the fourth presented with subarachnoid hemorrhage from an aneurysm on the posterior communicating artery of the opposite side, and the fifth case had an extensive infiltrating glioma.

These 5 cases were encountered in the course of approximately 1,500 arteriographies. Other investigators have found this anomaly with slightly less or slightly greater frequency; hence, it is not excessively uncommon.

Roentgenologically, a full-axial view is recommended in trying to demonstrate the exact appearance of the anomalous vessel. With a half-axial view the apex of the basilar artery and the vessels arising therefrom are obscured by the anterior cerebral artery.—*Samuel G. Henderson, M.D.*

Begg, A. C. Radiographic demonstration of the "hypoglossal artery"; a rare type of persistent anomalous carotid-basilar anastomosis. *Clin. Radiol.*, July, 1961, *12*, 187–189. (From: The Department of Diagnostic Radiology, Dunedin Hospital, and The Otago Medical School, Dunedin, New Zealand.)

The basilar artery may arise from the posterior aspect of the cervical portion of the internal carotid artery. This represents a persistence of certain small anastomotic channels linking the internal carotid and vertebral arterial systems in the embryo. Most writers have considered that this vessel represents the hypoglossal artery. It has been described previously on four occasions as a finding in anatomic dissections.

The author, discovered this anomaly on arteriography in a patient who later came to surgery for an inoperable brain tumor. This is apparently the first time that this anomalous artery has been found during life.—*Samuel G. Henderson, M.D.*

Salinas, F. de los Santos, and Gayarre, M. Gil. La sialografía. Tecnica, indicaciones y resultados. (Sialography. Technique, indications and results.) *Acta ibér. radiol. cancerol.*, Apr.-June, 1960, *15*, 107–116. (From: Catedra de Radiología y Terapeutica Fisica de la Universidad de Madrid, Spain.)

The technique for contrast roentgenography of the parotid and submaxillary glands is described with great detail. The patient is asked to rinse his mouth with warm water (40°C.) in order to relax and dilate the distal end of the excretory ducts. The duct is dilated, if necessary, and catheterized with a blunt-end needle not more than 1 mm. in diameter. For a contrast medium, the authors much prefer iodized oils to aqueous media. They inject 1.5 to 2 cc. in the submaxillary gland and 2.5 to 3 cc. in the parotid until the patient experiences pain and distention of the gland is noted. With the needle in place to prevent reflux, roentgenograms are taken. The needle is withdrawn and excretion of the contrast medium is achieved by having the patient chew gum and rinse the mouth to eliminate the contrast medium in the oral cavity. Additional roentgenograms are obtained during this time. The best projection for visualization of the submaxillary gland is obtained with the roentgen-ray beam angled 60° from the vertical plane and the patient lying supine with the head rotated to the side being studied. For study of the parotid gland, lateral views are preferred.

The authors have found interesting features in cases of transparent calculi, chronic inflammations, fistulae, relapsing parotitis, Mikulicz's disease, benign and malignant tumors, actinomycosis, and in patients who have received irradiation for conditions in the region of the salivary glands.—*F. Comas, M.D.*

Neck and Chest

Rogan, J. M., Ashford, J. R., Chapman, P. J., Duffield, D. P., Fay, J. W. J., and Rae, S. Pneumoconiosis and respiratory symptoms in miners at eight collieries. *Brit. M. J.*, 1961, *1*, 1337–1342. (From: Pneumoconiosis Field Research, National Coal Board, London, England.)

This report on a project which was started in 1953 includes an investigation into the correlation of coal dust, pneumoconiosis, respiratory diseases, forced expiratory volume ($F.E.V._1$), and roentgen findings.

A total of 9,758 men from eight British collieries were examined. The prevalence of pneumoconiosis increased with age. It varied from 9 to 41 per cent from one colliery to another.

Prevalence of respiratory symptoms increased with age also. The mean $F.E.V._1$—that is, the volume of air expired during the first second of a forced expiration after a full inspiration—in men with respiratory symptoms was about .2 to .4 liter less than that in men without respiratory symptoms.

There was some relation between pneumoconiosis and respiratory symptoms. Respiratory symptoms were associated with a smaller fall in the $F.E.V._1$ in men with pneumoconiosis than in men with normal roentgenograms.

Irrespective of the presence or absence of pneumoconiosis and respiratory symptoms, the $F.E.V._1$ fell uniformly with age.—*David C. Aiftine, M.D.*

Robertson, A. John, Rivers, D., Nagelschmidt, G., and Duncumb, P. Stannosis; benign pneumoconiosis due to tin dioxide. *Lancet*, 1961, *1*, 1089–1093. (Address: A. J. Robertson, Royal Infirmary, Liverpool, England.)

In 1955, 121 patients were studied roentgenographically and were found to have peculiar densities on chest roentgenograms. The diagnosis was not confirmed, but was thought certainly to be a benign pneumoconiosis due to tin dioxide.

The lungs of 7 of these patients have been obtained from necropsy. This is a report of the findings after pathologic examination, chemical and x-ray-diffraction analysis, and x-ray-emission spectroscopy.

Although tin in various compounds is processed by these workers, it appears that when the ore is reduced and smelted, the hot gases from the molten metal are inhaled. This is thought to be the main cause of "stannosis" in the lungs.

In the 7 patients observed, there was no significant pulmonary fibrosis and no evidence of silicosis. Chemical and x-ray-diffraction studies showed that the lungs contained tin dioxide.

The authors confirmed the diagnoses, made six years previously, of benign pneumoconiosis due to tin dioxide.—*David C. Alftine, M.D.*

Semple T., and Lancaster, W. M. Noisy pneumothorax; observations based on 24 cases. *Brit. M. J.*, 1961, *1*, 1342–1346. (From: Victoria Infirmary, Glasgow, Scotland.)

A total of 24 patients with noisy pneumothorax in the past 10 years has been encountered. The patients have presented chest findings of clicking, crackling, or crunching sounds at the cardiac apex with left-sided pain.

The youngest were 4 youths of eighteen years. The oldest was a woman of thirty-six. Pain was severe initially, but gradually lessened within hours, while the noise often lasted days.

Eighteen patients had obvious pneumothorax on roentgenograms. In 4 others special studies were required in order to demonstrate the condition roentgenographically. In 2 patients no abnormality was noted, but expiratory roentgenograms were not taken.

Hamman's sign may be heard in traumatic or severe spontaneous mediastinal emphysema, but shallow left pneumothorax is much more frequently the cause. The authors list several serious conditions requiring differential diagnosis.

Noisy pneumothorax is a benign condition, usually occurring in young healthy males, and is invariably left-sided. In a healthy patient with sudden chest pain this diagnosis cannot be excluded unless a roentgenogram is taken in full expiration.—*David C. Alftine, M.D.*

Smart, M. J., and Spencer, E. W. Bronchiolar ectasia and bronchial gland dilatation. *J. Canad. A. Radiologists*, 1961, *12*, 56–62. (From: University Hospital, Saskatoon, Sask., Canada.)

The authors take exception to the idea "suggested in recent American literature" that bronchiolar ectasia and bronchial gland dilatation are uncommon. In a review of 161 consecutive bronchograms, 36 cases of mucous gland dilatation and 10 cases of bronchiolar ectasia were found. In 2 of the cases demonstrating both abnormalities, bronchiectasis was also present.

"Trapping" of contrast material (aqueous dionosil) within ectatic cavities on days subsequent to bronchography was found to be of diagnostic value in doubtful cases of bronchiolar ectasia.

The authors feel that the presence of both bronchiolar ectasia and mucous gland dilatation in the absence of bronchiectasis justifies the diagnosis of chronic bronchitis.—*W. C. MacCarty, Jr., M.D.*

Cornudella, R., Frechilla, L., Lorenzo, T., Margarit, F., Conti, J. Reventós, and Albertí, A. La función ventilatoria en las bronconeumopatías congénitas; estudio de 5 casos. (Pulmonary ventilation studies in broncho-pulmonary congenital anomalies; study of 5 cases.) *Ann. med.*, Oct., 1960, *46*, 516–530. (From: Departamento de Exploración Funcional del Servicio de Aparato Respiratorio del Hospital de la Santa Cruz y San Pablo de Barcelona, Barcelona, Spain.)

Five cases are reported with complete clinical, roentgenologic and pulmonary function studies. The cases include 2 aplasias of the left lung, a congenital cyst of the left lung secondarily infected with tuberculosis, a polycystic left lung and a congenital bronchiectasis of the left lower lobe.

It was found that there was a deficit in the pulmonary function in all cases. The deficit appears to be directly proportional to the precocity of the malformation and the amount of pulmonary tissue involved. The uninvolved lung appears to compensate partially by using its pulmonary reserve and increasing its output. This compensation appears to be about 15 to 30 per cent.—*Cesar E. Rosa Perez, M.D.*

Dragoni, G., and Galli, G. Le manovre di Valsalva e di Müller e la loro utilità nello studio radiologico di alcune manifestazioni patologiche del torace. (The utility of the Valsalva and the Müller maneuvers in the radiological study of thoracic pathologic

manifestations.) *Radiol. med.*, Mar., 1961, *47*, 193–207. (Address: G. Dragoni, Orio-Litta, Milano, Italy.)

The Valsalva maneuver consists of a prolonged forced and blocked expiration. The Müller maneuver is the inverse of the preceding and consists of a forced and blocked inspiration.

During the Valsalva maneuver there is: (1) an increase in pulmonary transparence; (2) a better definition of the arterial tree; (3) reduction of the venous perihilar shadows; (4) a reduction or loss of fogging because of the diminished filling of the alveolar capillaries.

The Müller maneuver is not particularly useful in the roentgenologic diagnosis of pulmonary parenchymal pathologic manifestations. It may, however, have value in the differentiation of pulmonary vascular from parenchymal lesions.

The Valsalva maneuver was adopted for: (1) the demonstration of parenchymal metastasis which might be obscured by the vascular pattern; and (2) the recognition of hilar and mediastinal lymphadenopathy which is rendered difficult, by the superimposition of vascular shadows.—*A. A. Blasi, M.D.*

Hemley, Samuel D., Arida, Edward J., Diggs, A. Monroe, and Freeman, Sumner L. Percutaneous cricothyroid membrane bronchography. *Radiology*, May, 1961, *76*, 763–769. (Address: S. D. Hemley, St. Luke's Hospital, Amsterdam Ave. and 113th St., New York 25, N. Y.)

This study is based on six months' experience with 42 consecutive transcricoid needle punctures for bronchographic examinations. The technique is described in detail. There were only three complications directly related to the procedure. In one patient subcutaneous emphysema developed but cleared in three days. A second patient experienced hoarseness for one day. A third patient developed a brisk hemoptysis presumably from severe tuberculous bronchiectasis, and death from cardiac arrest ensued during administration of anesthesia for bronchoscopy on the same day.

With absorbable contrast medium, antibiotic control, and careful attention to asepsis, the method appears to be safe, effective, and time saving, particularly for departments of radiology in large and busy general hospitals. The frequency and seriousness of the complications of this procedure appear to have been exaggerated in the past.

Since submission for publication, 43 additional studies have been performed with one minor complication, subcutaneous emphysema of the neck discovered on a routine 24 hour post-drainage study.—*Walter H. Jarvis, Jr., M.D.*

Garusi, G. F. Opacification of the bronchial arteries in the living; (a new method of experimental demonstration). *Radiol. clin.*, 1961, *30*, 65–75. (Address: Istituto del Radio dell'Università, Policlinica San Orsola, Bologna, Italy.)

Opacification of the bronchial arteries during angiocardiography or aortography is rare and rather poor. Visualization of the bronchial arteries appears to be limited to cases in which they have become dilated in response to the diminished pulmonary arterial circulation which occurs in chronic lung disease or cardiovascular disease.

The author has achieved better visualization of the bronchial arteries in dogs by performing retrograde thoracic aortography during acetylcholine induced cardiac arrest. He concludes that further experiments are necessary to define the possibilities and the practical importance of the method.—*J. L. Williams, M.D.*

Ormond, Robert S., Poznanski, Andrew K., and Templeton, Arch W. Pulmonary veins in congenital heart disease in the adult. *Radiology*, June, 1961, *76*, 885–893. (Address: R. S. Ormond, The Henry Ford Hospital, Detroit 2, Mich.)

The routine roentgenogram of the chest remains the base line for appraisal of the cardiac patient. The usual lesion encountered in congenital heart disease in the adult is monopathic; therefore, the radiologist can be quite accurate in his prediction of the abnormality. The present study is directed to an analysis of the pulmonary veins in congenital heart disease in adults, since the pulmonary veins reflect the flow of blood through the lung fields.

Four major venous channels are constant in position and can usually be identified on routine posteroanterior roentgenograms of the chest. They are: posterior division of the superior pulmonary veins, the superior and inferior divisions of the inferior pulmonary veins and the middle pulmonary veins. These vessels can be seen crossing the arterial channels and entering the left atrium below the main pulmonary arteries. No value can be ascribed to the diameter of a normal vein, because there is considerable variation in vein size in normal patients. With experience a reasonably accurate appraisal of the deviations from normal is possible. The authors utilize a classification which separates the veins into five categories: (1) definitely reduced; (2) reduced to normal; (3) normal; (4) normal to increased; and (5) definitely increased. This is a gross division and subject to inexactness but it is of value when the appearance of the veins is correlated with the arterial and the cardiac configuration.

Eighty-six patients were included in this study. Right heart catheterization was done in all, with determination of intracardiac, pulmonary artery, and pulmonary wedge pressures. The oxygen saturation

of the blood was determined at suitable levels in the heart and pulmonary artery. Ten of the patients had undergone selective angiocardiography and in 43 the lesions were confirmed at the time of corrective surgery or at autopsy.

In lesions such as pulmonary stenosis and pulmonary hypertension, leading to shunt balance and reversal, in which the cardiac output is reduced, the veins are small. In uncomplicated interatrial septal defect, the pulmonary veins are definitely increased in size. In patent ductus arteriosus with left-to-right shunt the veins are large. In cases with a balanced or a reversed shunt, the veins are smaller than those seen in normal patients and may approach the size of veins in severe pulmonary stenosis. In patients with pulmonary hypertension, a successful surgical result depends upon the presence of a significant left-to-right shunt. Vein size offers one more method of valuating the amount of such a shunt.—*A. W. Sommer, M.D.*

LEVIN, BERTRAM, and WHITE, HARVEY. Total anomalous pulmonary venous drainage into the portal system. *Radiology*, June, 1961, *76*, 894–901. (Address: B. Levin, Michael Reese Hospital, Chicago 16, Ill.)

Although many variations of anomalous pulmonary venous drainage are known, the majority is supradiaphragmatic with the veins emptying into the right side of the heart directly or via interposed vascular channels. Some of these can be suspected from the characteristic roentgenographic contour of the heart and great vessels. Total anomalous pulmonary venous drainage into infradiaphragmatic vessels is far less common, comprising 10 to 20 per cent of all cases, and the drainage is usually into the portal vein or ductus venosus. These patients, however, present a characteristic and distinctive roentgenographic appearance of the pulmonary vascular pattern, rather than the heart or great vessels, which permits accurate diagnosis.

Four cases of infradiaphragmatic total anomalous pulmonary venous return are presented, each with similar characteristic pulmonary vascular markings. All were cyanotic white male infants who expired at approximately two months of age. Diagnosis was established by angiocardiography in one case, and the 3 additional cases were proved by autopsy. In each instance the pulmonary veins joined to form a single trunk, which traversed the diaphragm either through the esophageal hiatus or a special hiatus just anterior to the esophagus, and emptied into either the portal system (3 cases) or the ductus venosus (1 case). The expected shunt was provided by a large ventricular septal defect in 1 case and a patent ductus arteriosus in the other 3. Two of the cases with a patent ductus also presented a patent foramen ovale.

The interesting and characteristic feature in each instance is a prominent mottled and finely reticulated appearance of the pulmonary vascular markings which extends to the periphery of the lung fields. Kerley lines can be identified in the lung bases, with varying degrees of clarity. These lines often are more apparent in the lateral view than in the frontal. In all cases the cardiac size and contour are not appreciably altered from the normal which differs from supradiaphragmatic anomalous drainage and other congenital cardiovascular diseases with pulmonary vascular engorgement. In 2 cases the antemortem diagnosis was made from the chest roentgenograms.

The authors, in conclusion, state that this anomaly might be amenable to surgical correction. Although the pulmonary venous trunk is a thin walled channel with varying degrees of scarring, it could be transplanted into the small left atrium which is known to be atrophic and not aplastic.—*Edward B. Best, M.D.*

ANDERSON, I. M., and COLES, H. M. T. Endocardial cushion defects. *Brit. M. J.*, Mar. 11, 1961, *1*, 696–705. (From: The Westminster Hospital, London, England.)

Misdiagnosing an endocardial cushion defect as a simple ostium secundum patency may be serious because the former cannot always be corrected surgically without the use of extracorporeal circulation. The authors quote Bailey *et al.* and Watkins and Gross as stating that 10–15 per cent of cases operated for atrial septal defects have this more complicated lesion.

They briefly discuss the embryology and subscribe to the terminology used by Campbell and Missen. Thus, a Grade I defect includes persistence of the ostium primum with splitting of the anterior mitral cusp or the septal cusp of the tricuspid valve, or both; Grade II includes, with the ostium primum, bifid atrioventricular valve cusps and a high ventricular septal defect; and Grade III includes those with persistence of the common atrioventricular canal.

Symptoms include failure to thrive, dyspnea, respiratory infections and, commonly, cyanosis and heart failure. These occur fairly early and the prognosis is poor. A widely radiating holosystolic murmur is the rule with a mid-diastolic murmur often associated; a thrill may be present.

The authors feel that chest roentgenography often fails to differentiate these lesions from other septal defects with a predominant left to right shunt. They consider that the electrocardiographic pattern is highly characteristic and that catheterization is helpful. Angiocardiography is a definite diagnostic aid. They present 10 cases of this lesion with 2 cases of large ostium secundum defects which were misdiagnosed as the above. Of the 10 cases, 5 died (without surgery) of pneumonia and/or congestive failure. Of 5 which were surgically corrected, 3 are

living and well. Both ostium secundum defects were repaired with 1 of the patients dying.—*William H. Baker, M.D.*

Genitourinary System

Don, Conway. Asymmetry of the kidneys in disease of the main renal artery. *J. Canad. A. Radiologists*, Mar., 1961, *12*, 15–21. (From: The Ottawa General Hospital, Ottawa, Ontario, Canada.)

In a series of 100 normal intravenous pyelograms in patients with normal blood pressures, the author attempted to determine what degree and type of asymmetry can be accepted as a normal variant. In contrast to the normal cases, there were 6 cases with asymmetry in which disease of the main renal artery was shown by aortography at operation or at postmortem examination.

It is recognized that there is normal asymmetry of the kidneys, the right kidney being shorter and thicker than the left. In addition to evaluating the length of the kidneys, the author determined the thickness of the parenchyma by measuring from the tips of the papillae to the nearest portion of the renal outline, at midlevel.

It was found that in 73 per cent of the cases there was less than 1 cm. difference in length between the kidneys of the same subject. In 27 per cent there was asymmetry of 1 cm. or over. It was decided that asymmetry in length alone was of no significance. In the control series, when the kidney was 1 cm. or more shorter, the renal parenchyma was usually thicker. It was therefore concluded that, if asymmetry in length is accompanied by parenchymatous thinning of the shorter kidney of 3 mm. or more, this is suggestive evidence of main renal artery disease, and an indication for aortography. It is important, however, to be aware of the fact that absence of these findings does not preclude a renal artery lesion.—*J. N. Ané, M.D.*

Sutton, David, Brunton, F. J., and Starer, F. Renal artery stenosis. *Clin. Radiol*, Apr., 1961, *12*, 80–90. (From: Diagnostic X-ray Department, St. Mary's Hospital, London W.2, England.)

Renal artery stenosis is now recognized as a significant cause of hypertension. In over 1,000 examinations by aortography for conditions such as aortic thrombosis, iliac stenosis or abdominal aneurysm, the authors have seen 20 cases of renal artery stenosis, usually as a chance finding. In this group, 11 individuals were known to have hypertension and 5 were known to be normotensive. As part of the investigation of 260 known hypertensives who were subjected to arteriography for the purpose of finding or excluding renal artery stenosis or other vascular disease, 26 cases of renal artery stenosis were encountered. Nine cases of stenosis were shown by selective renal arteriography and 17 by direct aortography.

Aortography may be performed using three different techniques. The first is simple translumbar aortography; the second is aortography by percutaneous transfemoral catheterization; and the third is percutaneous selective renal aortography in which the opaque catheter tip is guided into the renal artery under fluoroscopic control. The particular method used is largely a matter of personal experience and preference. The selective method undoubtedly produces the most detailed demonstration of the renal vascular tree with minimal injections of contrast material, but it may be technically impossible to perform in cases of multiple renal arteries.

The most serious side effects reported in the literature have been renal damage and paraplegia, and there is little doubt that most of them have been due to excessive doses of contrast medium. The authors use 20 cc. of 76 per cent urografin as a maximum dose for free injections into the aortic lumen, and it is possible to obtain adequate visualization with lower doses. For selective renal angiography they generally inject 5 cc., or less, of 45 per cent hypaque or 60 per cent urografin. Great caution is necessary in the presence of impaired renal function, either bilateral or unilateral. The hypertension itself is an added hazard as it increases the tendency to hemorrhage and to the formation of large hematomas.

The highest incidence of renal artery stenosis is in patients over forty years of age. The increased frequency in males reflects the predominance of atheroma in men.

The lesions have been grouped into four grades of severity, determined by the degree of encroachment on the arterial lumen as seen on the angiograms. The stenosis is usually shown as a smooth narrowing of the lumen of the artery, and is nearly always less than 1 cm. in length, usually only 2 to 4 mm. The presence of post-stenotic dilatation of the renal arteries was noted 19 times. The stenosis occurred at the origin of the renal artery or within 1 cm. of it in 36 instances. Good demonstration of the origin of the renal arteries will show or exclude the majority of stenoses, although the origin of one or other of the renal arteries is frequently obscured by the superior mesenteric artery.

Certain clinical features may suggest the presence of renal artery stenosis: (a) unexplained hypertension in a young adult; (b) the sudden onset of malignant change in a patient known for years to be a hypertensive; (c) hypertension occurring in a patient with known general atheromatous disease; and (d) the presence of an upper abdominal bruit in a hypertensive patient.

The importance of changes on the plain roentgenogram and pyelogram in cases of renal artery stenosis is stressed. The affected kidney is smaller than the contralateral one. The contrast material may be in greater concentration on the affected side, and its

excretion may be demonstrably less in quantity. The calyces may appear relatively "spastic" on the affected side. This last-mentioned finding is frequently seen on intravenous pyelograms. When it occurs bilaterally, the most common cause is considered to be overenthusiastic dehydration of the patient in the preparation for pyelography. It reflects the low urinary output, and the appearance is due to underfilling of the calices rather than to "spasm." When seen on one side only, it may be due to other causes, such as inflammatory lesions and calculi.

In 1 case seen on referral, renal artery stenosis on the left side was suggested because of poor contrast on this side together with an alleged left-sided bruit. Arteriography showed a normal left renal artery and stenosis of the right renal artery. Repeat intravenous urographic examination after strict water deprivation for twelve hours showed a much less marked difference in the contrast values between the two kidneys. The appearances described are clearly due to the fact that the ischemic kidney continues to excrete a concentrated urine under conditions of water load, while the contralateral kidney produces a very dilute urine.—*Samuel G. Henderson, M.D.*

PALUBINSKAS, A. J., and WYLIE, EDWIN J. Roentgen diagnosis of fibromuscular hyperplasia of the renal arteries. *Radiology*, Apr., 1961, *76*, 634–639. (Address: A. J. Palubinskas, Department of Radiology, University of California Medical Center, San Francisco 22, Calif.)

Fibromuscular hyperplasia of the renal artery has recently been reported as a cause of renal artery stenosis and secondary hypertension. The etiology of the lesion is unknown. It has been suggested that the hyperplasia may be secondary to chronic stretching of the renal artery in patients with kidneys that are more mobile than usual.

Renal arteriography is the definitive diagnostic examination. The involved artery presents a distinctive appearance at arteriography. It may have an irregular appearance resembling a string of beads; constricted areas may be single but are more often multiple; post-stenotic dilatation of the renal artery or its branches may occur, with the occasional formation of a berry aneurysm. Fibromuscular hyperplasia appears to involve primarily the middle and/or distal third of the renal artery and may extend into the proximal branches of the main renal artery.

The authors report 11 patients with fibromuscular hyperplasia of the renal arteries seen within a two year period. The patients were all females between fifteen and forty-nine years of age, with hypertension known to have been present one week to twelve years. To date, 9 of the patients have been explored surgically. In each, the stenotic lesion in the renal artery was found to be due to hypertrophy of the muscular elements and, to a lesser extent, to the fibrous connective tissue elements of the media of the vessels. Arterial reconstructive procedures were performed in all cases except 1 in which nephrectomy was done. Following operation, the blood pressure returned to normal levels in 5 and decreased significantly in 3 patients.—*Arno W. Sommer, M.D.*

WITCOFSKI, RICHARD L., WHITLEY, JOSEPH E., MESCHAN, I., and PAINTER, WILLIAM E. A method and parameters for the analysis of renal function by external scintillation detector technic. *Radiology*, Apr., 1961, *76*, 621–627. (Address: R. L. Witcofski, Bowman Gray School of Medicine, Winston-Salem 7, N. C.)

With the advent of ortho-iodohippuric acid I^{131} (OIHA), better scintillation renograms have been obtained. It is now possible to compare right and left curves with greater confidence, and theoretically to quantitate renal function. Various methods of analysis are possible.

The authors' method included renography, blood and bladder activity studies at thirty minutes, and a chart recording of blood activity. The main and plateau times of the vascular phase are determined, as are half-secretory and excretory times; and blood clearance can be calculated.

Details of equipment and techniques are presented.

Parameters expressing the rates of secretion, excretion, and total renal function are given, as well as the normal values, including those for clearance studies.—*James C. Moore, M.D.*

DAMANSKI, M. Cysto-urethrography in paraplegia: its practical application. *Brit. J. Urol.*, Mar., 1961, *33*, 67–75. (From: The Liverpool Regional Paraplegic Centre, Promenade Hospital, Southport, England.)

Paraplegics are very prone to urinary difficulty and cystourethrography is a valuable means of investigating the cause of urinary retention.

The author describes his technique. The bladder is emptied with a catheter and 8 fluid oz. of 10 per cent sodium iodide solution are injected, using a Riches syringe. One anteroposterior and 1 oblique roentgenogram are taken. Following this, a few ounces of the same contrast material are injected into the external meatus and anteroposterior and oblique roentgenograms are obtained; this study visualizes the urethra. Finally, a roentgenogram is taken of the upper urinary tract to investigate reflux.

The author believes that any significant obstruction of the bladder neck or urethra will be demonstrated by this examination. Different sites of obstruction between the bladder neck, external sphincter, and posterior urethra are visualized. If the patients do not improve following surgery, the examination is repeated.

Other abnormalities may be seen, such as diverticula of the urethra or bladder and other evidences of obstruction and infection.

The author feels that this is a very valuable examination in the urologic work-up of paraplegics.—*George L. Sackett, Jr., M.D.*

Kirkland, J.A., and Haslock, Margaret Rae. Transient proteinuria; following intravascular injection of contrast media. *Lancet*, Apr. 1, 1961, *1*, 693–695. (From: The Department of Pathology, University of St. Andrews [Queen's College], and the Royal Infirmary, Dundee, England.)

Because of numerous reports of renal complications, including massive albuminuria following aortography, the authors investigated the occurrence of proteinuria in 53 patients subjected to intravenous pyelography and 14 to aortography.

Results after Intravenous Pyelography. Proteinuria before injection was found in 16 patients and, of these, 3 became more positive following injection; the remainder were unchanged. Seven of the remaining 37 developed proteinuria, most of them to a slight degree varying from 30 mg./100 ml. to 300 mg./100 ml. One had massive proteinuria of 1,000 mg./100 ml. This proteinuria lasted for two days in most patients, but in 2 it persisted for four days.

Results after Aortography. The first 4 patients were examined by translumbar injection with 70 per cent pyelosil and all of these showed a massive proteinuria—from 730 mg. to 1,300 mg./100 ml. The remaining 10 cases were examined by retrograde catheterization of the femoral artery using 70 per cent urokon as a contrast medium and only 1 of these patients had proteinuria, which was slight (100 mg./100 ml.).

The method of testing for protein in the presence of radiopaque contrast material is discussed and the authors recommend the paper strip tests "Albustix" and "Uristix," which do not give false positive results under these conditions.—*George L. Sackett, Jr., M.D.*

Skeletal System

Dahlin, David C., Coventry, Mark B., and Scanlon, Paul W. Ewing's sarcoma; a critical analysis of 165 cases. *J. Bone & Joint Surg.*, Mar., 1961, *43-A*, 185–192. (From: The Section of Surgical Pathology, the Section of Orthopaedic Surgery, and the Section of Therapeutic Radiology, Mayo Clinic and Mayo Foundation, Rochester, Minn.)

Ewing's sarcoma is a highly malignant primary tumor of bone occurring chiefly in the second decade of life and affecting almost any bone. Because the nature of the parent cell is still in marked dispute, the eponym "Ewing's Sarcoma" must still remain to distinguish this specific entity.

For many years after Ewing's original description, the pathologic diagnosis of the condition was indefinite and a variety of neoplasms and some nonneoplastic conditions were included under this diagnosis. With recent advances in the knowledge of bone pathology, the diagnosis is now made with greater exactitude. Ewing's sarcoma may be defined as a highly anaplastic, malignant, small round cell tumor which is primary in bone and usually can be readily differentiated from other small round cell tumors. Occasionally, highly malignant tumors are observed in which the size and morphologic characteristics of the nuclei are intermediate between those of Ewing's sarcoma and those of reticulum cell sarcoma. In such instances, correlation with the clinical findings serves to determine the correct classification. The small cells of Ewing's sarcoma characteristically occur in large islands which contain little or no connective tissue. Grossly, the tumor cannot be definitively distinguished from other tumor or, at times, from inflammatory processes.

The authors report a study of 165 patients with Ewing's sarcoma seen at the Mayo Clinic from 1905 to January 1, 1960, a group comprising somewhat less than 10 per cent of the total number of primary malignant bone tumors seen during the same period. In location, the femur was the most common site, being involved in slightly more than one fourth of the group; approximately three fourths of the tumors occurred in the pelvic girdle and long tubular bones of the extremities. Contrary to the widely-held tenet that Ewing's sarcoma characteristically involves the diaphysis of long bones, it was found that the metaphyseal region was more commonly the epicenter of the growth. In age, the youngest patient was eighteen months and the oldest fifty-nine years. Nearly half of the cases occurred in the second decade and almost 90 per cent within the first three decades. Males predominated by a ratio of 101:64.

Whereas in the past the roentgenographic appearance was considered to be relatively pathognomonic, characterized by osteolysis without osteosclerosis and by an onion-skin layering of the subperiosteal new bone, it was determined in this review that the findings were extremely variable and not specific. Many of the lesions contained zones of sclerosis. Radiating spicules from the cortex of the affected bone were not uncommon. The appearance of Ewing's sarcoma could be mimicked by several other malignant tumors, as well as by eosinophilic granuloma and osteomyelitis. The definitive diagnosis, therefore, had to depend on microscopic examination.

Treatment consisted of irradiation, amputation, local excision, curettage, and Coley's toxins in a wide variety of combinations and for this reason it was difficult to evaluate the effectiveness of any one specific form of treatment. Of 79 patients with

sarcomata in the extremities treated before 1955, 48 received irradiation as the first definitive therapy and 18 underwent amputation as the first measure. The over-all five year survival was 15 per cent and the ten year survival was 10 per cent; 45 per cent of the patients died within the first year and 70 per cent were dead by the end of the second year.

No definite conclusion could be drawn regarding the relative effectiveness of irradiation and ablative surgery. Irradiation was of great value as a palliative measure, particularly for pulmonary metastases, 2 patients surviving more than twenty years after such therapy.—*Leslie K. Sycamore, M.D.*

RALSTON, E. L. (Philadelphia, Pa.) Legg-Calvé-Perthes disease—factors in healing. *J. Bone & Joint Surg.*, Mar., 1961, *43-A*, 259–265.

The author reports an analysis of 43 children with unilateral Legg-Calvé-Perthes' disease recognized within three months of onset and treated by a standard method throughout the course. The date of onset is assumed to be the date of the first symptom; the end point is defined as that time at which there is replacement by new bone in the capital epiphysis to the extent that a complete well-defined subchondral layer of bone is visible on both anteroposterior and lateral roentgenograms, and any defect remaining in the epiphysis does not constitute more than 25 per cent of the epiphysis. It is recognized that some degree of remodeling of the head and neck continues up to the time of epiphyseal closure, but the definition permits a precise and standardized period for comparative study.

Chronologic age of the patients varied from four to eleven and one half years with most of the cases falling between four and seven years. Retardation of skeletal age averaged one year and nine months.

Percentage of involvement of the epiphysis, with the author's method of measuring on the roentgenograms, varied from 10 to 100 per cent, with the greatest incidence falling between 50 and 80 per cent. Only 1 case showed complete necrosis of the epiphysis. The duration of the disease varied from eight to fifty-nine months, a wider range than reported by most authors. The largest number of cases fell between twenty and thirty-five months. The degree of recovery, as measured by the comprehensive quotient of Heyman and Herndon, varied from 65 to 100 per cent, with the largest number falling in the 80 to 85 per cent group.

Study of the correlation of the various factors brought out several conclusions somewhat at variance with generally accepted principles. Whereas it has been frequently asserted that the younger the child the more quickly will the disease run its course, in this series there was only a weak correlation. Controverting the theory that the end result is better in the younger child, no such correlation was present between these two factors in this series. A weak correlation existed between the age at onset and the degree of involvement of the epiphysis, the greatest percentage of involvement occurring in the older patients. A high degree of correlation was shown between the extent of involvement of the epiphysis and the duration of the disease, but only a weak correlation was shown between the involvement and the final comprehensive recovery quotient.

The author concludes with a plea for judging the results of treatment on a careful analysis of the roentgen findings rather than on clinical impressions. —*Leslie K. Sycamore, M.D.*

PONSETI, IGNACIO V., and COTTON, RALPH L. Legg-Calvé-Perthes disease—pathogenesis and evolution; failure of treatment with l-triiodothyronine. *J. Bone & Joint Surg.*, Mar., 1961, *43-A*, 261–274. (From: The Department of Orthopaedic Surgery, State University of Iowa, Iowa City, Ia.)

The authors observed that the epiphyseal plate lesion in Legg-Calvé-Parthes' disease was similar to the lesion observed in rats and rabbits fed diets containing aminonitriles. Since low doses of l-triiodothyronine suppressed the mild forms of aminoacetonitrile poisoning in rats, it was decided to test the effect of this compound on children with Legg-Calvé-Perthes' disease. Forty-four children of the same age and sex and with similar involvement of the hip were paired, one member of each pair receiving treatment with l-triiodothyronine. Similar orthopedic treatment was used in all cases. The period of treatment with the drug lasted from six to eighteen months.

Biopsy specimens revealed that the bone of the femoral head was necrotic and the epiphyseal plate cartilage was fibrillated and cracked. It was surmised that loss of the blood supply to the femoral head results from the interruption of the retinacular vessels when they cross the cartilage at the edge of the disrupted epiphyseal plate. With revascularization, the dead bone is replaced by living bone, either by the process of creeping substitution or by absorption of the necrotic bone by an advancing front of connective tissue, both processes often being intermingled. Direct creeping substitution is prevalent in the necrotic areas that are structurally well preserved, whereas abundant fibrous tissue is prominently observed adjacent to collapsed necrotic bone. On roentgenograms, structurally well-preserved dead bone is characterized by only slightly increased density. This density increases during the process of replacement by creeping substitution as new bone is laid down on the dead bone trabeculae. Collapsed areas appear on the roentgenogram as blotchy areas of increased density intermingled with more radiolucent areas.

In the earliest cases, the center of ossification of the femoral head is slightly denser and smaller than

on the normal side. Some collapse is present in all patients. An increase in the width of the space between the ossified portion of the femoral head and the inner wall of the acetabulum is observed in most early cases. Collapse occurs in the weight-bearing portion of the femoral head, the posterior portion being spared.

Reconstruction of the necrotic femoral head occurs according to three patterns. Group I (most common type): the posterior third of the epiphysis is rebuilt at a fast rate; the bone density is increased at first and gradually becomes normal in one or two years with new bone being laid down over the dead bone and then slowly replacing it over a period of one or two years; the anterior half ossifies much more slowly than the posterior half with several months elapsing between the absorption of the dense necrotic bone and the formation of radiolucent new bone; the epiphyseal plate is slightly wide and irregular. Group II: the pattern of reconstruction is initially similar to that in Group I; the collapse of the anterior two-thirds of the head, however, is very marked and, after absorption of the dead bone, this portion remains largely unossified for many months and even years. Group III: the bone of the entire femoral head collapses and reossification is very slow and irregular; small areas of new bone reconstruction appear at different sites after several months; the epiphyseal plate is wide and irregular, with large areas of decreased density extending deep into the metaphysis.

The final shape of the femoral head is normal in Group I, slightly flattened in Group II, and extremely flat in Group III. Determination of the degree of severity of the epiphyseal plate lesion is of great prognostic value, the speed of reconstruction being proportional to the severity of this lesion. The width of the femoral neck is increased in all cases, presumably owing to the increase in periosteal new bone formation along the neck. The primary lesion in Legg-Calvé-Perthes' disease appears to be a weakening and disruption of the upper femoral epiphyseal plate. Aseptic necrosis of the femoral head results from the interruption of the retinacular vessels when they cross the cartilage at the edge of the disrupted plate.

Studies of protein bound iodine and of the uptake of active iodine reveal no evidence of thyroid disease and recovery is not altered by the administration of large doses of l-triiodothyronine during periods of from six to eighteen months.—*Leslie K. Sycamore, M.D.*

Brown, B. St.J. The radiologic features of bone changes in tuberous sclerosis with a case report. *J. Canad. A. Radiologists*, Mar., 1961, *12*, 1–9. (From: The Department of Radiology, The Montreal General Hospital, Montreal, Quebec, Canada.)

The author describes the roentgen features of tuberous sclerosis with particular reference to the bone changes. The combination of bone changes in the presence of brain lesions is virtually diagnostic of the condition. In the investigation of epilepsy, mental deficiency and abortive forms of tuberous sclerosis, roentgenograms of the extremities and skull may be of considerable diagnostic value.

Tuberous sclerosis occurs in the general population in about 1 per 150,000, and in institutions for epileptics and mentally defectives in about 0.6 per cent. Tuberous sclerosis is a defect in the histogenesis and organization of tissues with a tendency to the formation of hamartomas. In the literature reviewed by the author there were only four descriptions of pathologic bone lesions in definite cases of tuberous sclerosis.

The roentgen findings occur more frequently in the brain (calcification in 80 per cent), the kidney (tumor-like nodules in 80 per cent), and the hands and feet (cyst-like changes, subperiosteal new bone and cortical pitting in 66 per cent). Patchy areas of increased bone density occurred in the upper halves of the parietal bones in 48 per cent. Less frequently noted were patchy areas of increased bone density in the pelvis and spine. Sclerotic patches and, more rarely, fibrocystic changes were noted in the long bones and ribs.

The differential diagnosis between tuberous sclerosis and osteosclerotic metastases is dependent upon the presence of other types of associated bone changes in tuberous sclerosis. Brain calcification aids considerably in the differential diagnosis.—*J. N. Ané, M.D.*

General

Bistolfi, F., and Pignataro, E. Rapporti fra spessore di strato e nitidezza d'immagini in stratigrafia pluridirezionale. (Relation between thickness of the layer and clearness of the images in multidirectional stratigraphy.) *Radiol. med.*, Dec., 1960, *46*, 1127–1149. (From: Istituto di Radiologia dell'Università di Genova, Italy.)

The recurring problem of the choice of layer thickness in laminagraphy was demonstrated at the last International Congress of Radiology, held in Munich in 1959, where Frain and Gaucher spoke in favor of thin layers and Westra and Ziedses des Plantes in favor of thick layers.

This paper deals with the effect of various layer thicknesses on the clearness of the images in multidirectional laminagraphy. It is based on practical experiments conducted for the past two years in the Institute of Radiology of the University of Genoa, under the guidance of Prof. A. Vallebona.

The technical characteristics of multidirectional laminagraphy can be summarized as follows: (1) shading-off of a material point in a chosen surface; (2) lack of transport shadows; (3) a more complete

shading off of images than that obtained in unidirectional laminagraphy, resulting in a greater elimination of shadows which are in other layers; (4) longer exposure time (the minimum, in the Pluristrator Zuder used by the authors, is 1.8 sec.); and (5) accurate portrayal of the images in the chosen layer.

The authors have adopted multidirectional laminagraphy in the evaluation of certain parts of the skeletal system, such as articular surfaces, canals and foramina, formations and ossicles of the inner and middle ear, the interruptions along the walls of certain bones (as in the petrous pyramids), mastoid cells (small cells) and paranasal sinuses (large cells), mucosa of the sinuses, and the spongiosa of long and short bones.

From these studies of the skeleton the authors conclude that a thick layer of 5 to 8 mm. gives a clearer image of the structures on the laminagram. The only exception to this general rule is noted on the laminagrams of the spongiosa of the vertebral bodies.—*A. F. Govoni, M.D.*

Campbell, John A., Klatte, Eugene C., Gray, Donald D., and McCrea, Alice L. Evaluation of film size in cineradiography. *Radiology*, April., 1961, *76*, 606–613. (Address: J. A. Campbell, Indiana University Medical Center, 1100 West Michigan Street, Indianapolis 7, Ind.)

Limited image detail remains the most critical obstacle to be overcome if cineroentgenography is to have a wider range of diagnostic usefulness.

The authors evaluate the relative merits of film size alone as a determining factor in the quality of a cine-image. In order to do this, other factors must be controlled: the resolving power of the image tube, image-tube focus, scintillation effect, relative speed of the lens system and focal spot of the roentgen-ray tube.

Image quality is judged by its resolution and its sharpness of detail. The greatest spatial frequency or the narrowest bars and spaces that can be resolved by the use of test objects is said to be the resolving power limit. The various test objects which may be used are the wire screen, General Electric lead reticle, Ter-Pogossian contrast test object, Phillips electric brass reticle, and the Indiana University test pattern used by the authors. This test pattern consists of diverging and converging bars and spaces of varying lines per inch. This arrangement allows testing of the edges of the field as well as the center.

Resolution tests were carried out using various popular 16 and 35 mm. film emulsions with this test pattern and, for comparison, with wire screen cloth and the General Electric lead bar reticle.

The authors conclude that, in clinical cineroentgenography using currently available image intensifiers, medium and fine grain 16 mm. film emulsions can be expected to produce images of diagnostic quality equal to those obtained with fast, coarse grain 35 mm. emulsions with the same radiation dose to the patient.—*W. M. McBride, M.D.*

Boucek, Robert J., Murphy, William P., Jr., and Hernandez, Francisco A. Intercalative angiography; cardiovascular spot-filming. *Radiology*, Apr., 1961, *76*, 565–571. (Address: R. J. Boucek, 1550 N. W. Tenth Avenue, Miami 36, Fla.)

Intercalative angiography or cardiovascular spot-filming is the electronically controlled spot-filming of an opacified portion of the cardiovascular system through the use of electronic devices which are activated by the electrocardiogram to trigger a rapidly acting injector and to trip off the roentgen ray exposure in a predetermined time sequence. Because the volume of the injected radiopaque material is small, high speed injections must be made via a catheter introduced into the area to be visualized so that the bolus of material will be imposed between or within a cardiac cycle, thus producing a discrete localization of the substance at the selected site. This obviates most of the limitations of the standard cardiovascular roentgen-ray procedures and eliminates unnecessary irradiation. In addition, repeat injections may be made during one examination.

A more detailed discussion of the apparatus and the technique, including a few illustrative roentgenograms, is presented.—*Walter H. Jarvis, Jr., M.D.*

Uhr, Nathaniel, and Bezahler, Harvey B. Pseudo-pseudohypoparathyroidism: report of three cases in one family. *Am. Int. Med.*, Mar., 1961, *54*, 443–451. (From: The C. F. Menninger Memorial Hospital, Topeka, Kan.)

Pseudohypoparathyroidism (PH) was a term used in 1942 by Albright *et al.* to describe a group of patients with round face, short stature, short metacarpals and metatarsals, ectopic ossifications, high serum phosphorus and low serum calcium. This disease is distinguished from idiopathic hypoparathyroidism by failure of the patients to respond to parenteral parathyroid extract with an increased urinary excretion of phosphate. Ten years later Albright described a case with many of the clinical features of PH, but with normal values for serum phosphorus and calcium. He termed this pseudo-pseudohypoparathyroidism (PPH).

The familial tendency of this disease has been noted and the authors report 3 patients, a mother and two sons, meeting most of the clinical and chemical criteria of PPH. Six other cases, first and second cousins of the patients, appeared to bear many superficial resemblances to the reported cases.

The interesting question of the terminology for these diseases is discussed as well as the inter-rela-

tionship between PPH and PH and the probable mode of inheritance.—*George L. Sackett, Jr., M.D.*

RADIOISOTOPES

Sterling, Kenneth, and Tabachnick, Milton. Resin uptake of I^{131}-triiodothyronine as a test of thyroid function. *J. Clin. Endocrinol. & Metabol.*, Apr., 1961, *21*, 456–464. (From: The Department of Internal Medicine, New York State Psychiatric Institute, and the Department of Psychiatry, Columbia University, College of Physicians and Surgeons, New York, N. Y.)

Since Hamolsky and Freedberg and their associates first announced the I^{131} triiodothyronine red blood cell uptake as a measure of the amount of circulating thyroid hormone, many groups have attempted to simplify the test by exposing the patient's serum to an adsorptive resin rather than erythrocytes.

The test described by the authors, while not a simple one to perform, seems the best resin test yet suggested. For those interested in performing it this interesting paper should be read in its entirety, but briefly the method is as follows. The resin IRA-400, one of the amberlite family of resins, is converted from the chloride form, in which it is supplied, to the formate form by washing with 1 M sodium formate solution adjusted to pH 5.0 ± 0.2. The resin is washed until free of chloride ion and stored at 5° C. under sodium formate solution. The resin appears to be stable for at least four months in this form. All operations until the final washings and count are carried out at a temperature of 2–6° C. Two ml. of test serum is added to 0.2 ml. of a solution containing an amount of I^{131} l-triiodothyronine with no more than 0.2 μg. per ml., and with a specific activity appropriate to the counting apparatus used. After shaking in a cold bath for 15 to 45 minutes, 1 ml. aliquots of the serum-triiodothyronine solution are added to tubes containing 1 ml. of washed resin and shaken for 90 minutes at the low temperature. Only during counting are the samples not maintained at a cold temperature. It is pointed out that warming to room temperature is to be avoided, since this increases the resin uptake. In the authors' laboratory, duplicate determinations on a given serum usually agree within 1 to 2 per cent as do the values for a given serum run at different times.

The authors tested the procedure in 35 normal patients and 44 patients with active thyrotoxicosis. Twenty-eight typical cases of myxedema and hypothyroidism were also tested, and values were determined for 11 pregnant women.

Results in the uptake of I^{131} triiodothyronine were: in hypothyroidism, 27 ± 3.3 per cent; euthyroid subjects 35 ± 2.2 per cent; thyrotoxicosis 53 ± 7.8 per cent. In pregnancy these values were depressed to the hypothyroid level or lower. Differences were found to be statistically significant, and apparently more reliable than duplicate determinations of erythrocyte uptake, and then the results by the resin test described by Mitchell. In cases of low TBG, as in the nephrotic syndrome, there is an elevated resin uptake even though the concentration of free thyroxine is normal and the patient is euthyroid. As with other tests of this family results are not influenced by contamination with organic or inorganic iodine.—*Frederick J. Bonte, M.D.*

Bowers, C. Y., Murison, P. J., Gordon, Douglas L., and Locke, William. Effect of thyrotropin on the serum protein-bound iodine level in various thyroid states (TSH-PBI test). *J. Clin. Endocrinol. & Metabol.*, Apr., 1961, *21*, 465–471. (From: The Departments of Medicine, Louisiana State University School of Medicine, Ochsner Clinic, and Tulane University School of Medicine, New Orleans, La.)

Single intramuscular injections of thyroid stimulating hormone (TSH) were administered to 22 normal subject and 67 patients with thyroid disease, including secondary myxedema. Resulting changes in the serum protein-bound iodine (PBI) concentration were measured. Twenty-four hours after injection of 5, 10 or 20 units of TSH the mean rises in PBI concentration for normal subjects were 1.3 μg. ±0.6 to 2.8 μg. ± 1.0 per ml. In general, rises were abnormally low in patients with diffuse thyroid disease, whereas they were normal in patients with focal thyroid disease or pituitary failure. In some of the patients who had nontoxic nodular goiter, responses were abnormally high. The significance of this phenomenon is not understood.

Because of the fact that TSH raises the PBI and thyroidal I^{131} uptake so little in patients with thyroiditis, the authors suggest the use of a TSH-I^{131} or TSH-PBI test to differentiate Hashimoto's disease from other nontoxic nodular goiters.—*Frederick J. Bonte, M.D.*

Deller, D. J., Germar, H., and Witts, L. J. Effect of food on absorption of radioactive vitamin B_{12}. *Lancet*, Mar. 18, 1961, *1*, 574–577. (From: The Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, England.)

Baseline determinations were made by administering Co^{58} labelled vitamin B_{12} to 5 normal volunteers, 5 hospital patients with disease not associated with absorption of vitamin B_{12}, 5 patients with pernicious anemia and remission, and 21 patients who had had a partial gastrectomy for peptic ulcer one to eighteen years before the test. These tests were performed in the fasting state, as usual.

The tests were repeated in all of these individuals by giving a test dose of Co^{58} vitamin B_{12} with a vitamin B_{12} free meal.

In the 10 normal subjects and in the 5 who had pernicious anemia the administration of food had no effect, but in the group of patients who had undergone partial gastrectomy the absorption of Co^{58} vitamin B_{12} was significantly enhanced when the test dose was given with food. In some patients in whom the absorption of vitamin B_{12} was grossly subnormal the effect of food was comparable with that of the intrinsic factor. The authors, therefore, conclude that the administration of a fasting dose of radioactive vitamin B_{12} is not a reliable method for determining the ability of the patient to absorb vitamin B_{12} when gastrectomy has been performed.—*Frederick J. Bonte, M.D.*

DUGGAN, H. E., and WEIJER, DOROTHY L. Results of treatment of malignant neoplastic disease with radioactive colloidal gold(Au^{198}); an analysis of 60 cases. *Canad. M.A.J.*, May 6, 1961, *84*, 1000–1003. (From: The University Hospital, University of Alberta, Edmonton, Alberta, Canada.)

Radioactive colloidal gold was first used intraperitoneally in 1947 by Hahn. Since then many reports of various workers have appeared in the literature. The method is especially suited for body cavity irradiation. The particle size, .003 to .007 μ in diameter, and the short half life make even irradiation possible with no damage to surrounding tissues. It has been used in the pleural and peritoneal cavity, in cystic brain lesions, and in the prostate.

This paper gives the results in 60 cases treated. The methods used are discussed and graphs showing the irradiation pattern are included. Good results occurred when the gold was used prophylactically at operation for carcinoma of the ovary with no demonstrable implants. However, these results are really not definitive, since the patients might have survived without this treatment.

The over-all results indicate that palliation was the main effect. It had no value in cases of carcinoma of the bronchus.

Sixty patients were treated by instillation of Au^{198} in an attempt to reduce or stop fluid production, diminish tumor size or prevent metastatic spread. Fifty-four had malignant effusions; 6 were treated prophylactically. There were 7 cases of prostatic carcinoma, and 3 of cystic brain tumors. Carcinoma of the ovary with ascites (25 per cent) showed good results with an average survival of nine months. The ovarian carcinomas without ascites showed good results in most cases (5 survived, 1 died). Carcinoma of the prostate (43 per cent) showed some improvement.

This paper is very informative. The results are about the same as those reported elsewhere—palliation only, but the procedure is one more modality of aid.—*Eva S. Carey, M.D.*

SARASIN, RAYMOND. Les complications de la télécobalthérapie. (Complications of telecobalt therapy.) *Radiol. Clin.*, Nov., 1960, *29*, 346–356. (From: Service de Radiologie de l'Hôpital Universitaire de Genève et du Centre de Télécobalthérapie, Geneva, Switzerland.)

The complications following treatment by high energy radiation did not differ significantly from those observed in conventional radiotherapy. Higher tissue doses, up to 8,000 r, may be employed in some cases, although usually for tumors such as those of the esophagus and bronchus only 4,000 to 5,000 r tissue dose is used for preoperative irradiation and this is usually given in five to seven weeks.

If a tumor which has extensively infiltrated the interstitial tissue is destroyed, this will leave a large region which needs filling in and may actually lead to complication. In addition, there are individual factors: certain patients seem to undergo necrosis while others treated with the same technique do not have any complications.

Preoperative irradiation is used whenever possible for the following reasons: (1) to diminish the degree of activity of the tumor; (2) to diminish the volume of the tumor, which may be of aid to the surgeon; (3) to utilize the more radiosensitive state of the tumor, which becomes less sensitive postoperatively because of changes in vascularity; and (4) to treat the general condition of the patient during irradiation, which, in turn, better prepares him for surgery. Also, patients can scarcely support the effects of irradiation after such operative procedures as pneumonectomy or extensive esophagectomy.—*Charles M. Nice, Jr., M.D., Ph.D.*

MISCELLANEOUS

LEE, J. A. H. Acute myeloid leukaemia in adolescents. *Brit. M. J.*, Apr. 8, 1961, *1*, 988–992. (From: Social Medicine Research Unit of the Medical Research Council, London Hospital, London, England.)

The death rate from leukemia is high in young children, and then falls to a minimum in early adult life. Previous studies show that, in males, the decline in the leukemia death rate during adolescence is interrupted by a transient rise. This excess mortality is not a new phenomenon, but has been observed at least as far back as 1911–15. A study of this phenomenon is now reported.

Analyses of the leukemia mortality data for England and Wales, Scotland, the United States, and for Canada were made. In each of these four countries the decline of the death rate stops at about the

age of 13 in males, and rises to a new peak at about 17. A further decline then occurs and continues until the late twenties. In females there is evidence of a similar trend, but it is less marked. In the United States and Canada the rise in the mortality rate in females appears to occur earlier than in males.

The data from England and Wales suggest that the death rate from leukemia in males aged 15–19 is about 6 per million per annum greater than would be expected if the trend of the rates with age were not interrupted in this period. The male population of this country in this age group is 1.4 million, so that the whole effect described in this paper is due to about 10 cases occurring annually. This figure gives a measure of the difficulty of studying the problem. However, the smallness of the numbers is due to the rarity of leukemia of any sort rather than to the smallness of the rate increase in adolescents. There is no evidence on which to base any discussion of the relationship of these cases of leukemia to radiation.

The high leukemia rates in male adolescents are matched by corresponding increases in admissions to hospitals for acute infections of the lower respiratory tract. In females the rise in the number of hospital admissions for these conditions is similar, but, as already pointed out, in England and Wales at least, the change in the female leukemia rate is less marked. These are interesting findings, because in children under the age of 10, Stewart (1961) has put forward evidence that pneumonia may induce leukemia after a short latent period.—*George Tievsky, M.D.*

Court Brown, W. M., and Doll, R. Leukaemia in childhood and young adult life; trends in mortality in relation to aetiology. *Brit. M. J.*, Apr. 8, 1961, *1*, 981–988. (Address: W. M. Court Brown, Director of the Medical Research Council's Clinical Effects of Radiation Research Unit, Western General Hospital, Edinburgh, Scotland.)

There is good reason to believe that the different clinical and cytologic types of leukemia represent distinct diseases. Thus, there are major differences between the age and sex distributions of chronic lymphatic, chronic myeloid, and acute leukemia. Furthermore, ionizing radiations have been shown to cause chronic myeloid and acute leukemia, but they have not been shown to cause chronic lymphatic leukemia, and the geographical distribution of the first two types differs from that of the last in that chronic lymphatic leukemia is relatively rare in the Far East. Finally, recent cytogenetic data have demonstrated the existence of a specific chromosomal abnormality in many cases of chronic myeloid leukemia, but, to date, not in any other type.

An analysis has been made of the mortality rates from leukemia among children and young adults under the age of 30 years in England and Wales during the period 1911–1959. Similar data for other countries have been examined over a shorter period.

Estimated mortality rates for acute lymphatic leukemia showed a maximum at the age of 3 years in both sexes. The mortality rate fell to a minimum at ages 25–29 years, with only a slight check at ages 15–19 years. The mortality from acute myeloid leukemia varied less sharply, but showed two peaks —at ages 2–4 years and 15–19 years. The reduction in the mortality figures for acute lymphatic leukemia in late adolescence and the peak in the childhood mortality rate from acute myeloid leukemia may be due to misclassification. The mortality from both types of chronic leukemia was low throughout the age range studied, but there was evidence of an increase in the mortality from chronic myeloid leukemia above the age of 20 years.

Between 1911 and 1959 the mortality increased fairly steadily in each five year age group and in each sex. The average rate of increase was approximately 4.5 per cent per annum under the age of 10 years and slightly less than 4 per cent per annum at ages 20–29 years. The age groups 0–4 years and 15–19 years showed no increase in the last 10 years. Part of the increase is likely to be spurious and due to such factors as better case-finding and improvements in the therapy of infections; but it is difficult to account for the continued increase at young adult ages by these factors alone. Data for the last 15 years suggest that there has been a real increase in chronic myeloid leukemia and in acute myeloid leukemia over the age of 15 years.

Before 1920 there was no evidence of a childhood peak in the mortality from leukemia. A peak mortality was present at ages 2–3 years from 1921 to 1939, and since 1940 the peak has become more pronounced. Mortality rates for the white population of the U.S.A. since 1940 have been similar, but at a higher level. Peaks in the childhood mortality have not been observed in the nonwhite population of the U.S.A. or in Japan.—*George Tievsky, M.D.*

Garland, L. Henry. Cancer of the thyroid and previous irradiation. *Surg., Gynec. & Obst.*, May, 1961, *112*, 564–566. (From: The Department of Radiology, University of California, Medical School and San Francisco General Hospital, San Francisco, Calif.)

The author compares statistics of several investigators and finds that the claim that previous irradiation about the nasopharynx and mediastinum contributes to development of carcinoma of the thyroid has no real proof. These comparative studies are impressive in their results.

Clark in Chicago encountered 13 cases of thyroid carcinoma in children who had a history of irradiation. The calculated dose was about 18–60 r. Uhlmann followed 480 of 2,500 children who had had previous irradiation and he found no carcinoma. Simpson and associates reported 1 case in an infant

to whom 3,000 r was delivered. This dose was obviously excessive and is conceivably related to the subsequent neoplasm. Snegireff was unable to find any cases of leukemia or thyroid cancer in cases with a history of previous irradiation. Latourette and Hodges studied 867 patients who had had thymic irradiation and they found 1 case of thyroid cancer contrasted to a normal expectancy of 0.06. Conti and Patton studied 1,564 irradiated cases. Evidence of subsequent carcinoma was thoroughly searched for and, even though 4 cases would normally be expected no case was found; 1 case of leukemia was expected but none was found.

The author estimates that during the years 1925 to 1945 at least 4,000,000 infants received irradiation to the mediastinum, either for treatment or during examination. The death rate for carcinoma of the thyroid up to 1958 has been static.

From a search of all available literature one must conclude that an etiologic connection between low dose neck irradiation and subsequent thyroid cancer cannot be regarded as established.—*Eva S. Carey, M.D.*

GALIBALDI, G., and GUGLIANTINI, P. Il problema del trattamento della iperplasia timica in rapporto ai supposti pericoli della roentgenterapia e ai risultati della cura medica. (The problem of treatment of thymic hyperplasia in relation to the supposed dangers of roentgen therapy and to the results from medical therapy.) *Radiol. med.*, Dec., 1960, *46*, 1159–1182. (From: Reparto di Radiologia Ospedale Pediatrico del Bambino Gesù, Rome, Italy.)

In the first half of this century the treatment for thymic hyperplasia was in the majority of cases limited to roentgen therapy; the first report dates back to a paper published by Friedlander in 1907 (Status Lymphaticus and Enlargement of the thymus with a Report of a Case Successfully Treated by the X-ray. *Arch. Pediatr.*, 1907, *24*, 490–501). In analyzing the several statistics on this matter the authors note that, at least in the United States, the highest peak in the use of this treatment was reached in the years 1932–1941 and that the number of cases so treated slowly diminished until, in 1950, roentgen therapy for thymic enlargement was almost completely abandoned. A similar attitude, although to a lesser extent, was noted in Europe.

The principal arguments against the use of ionizing radiation in the treatment of thymic enlargement are the following: (1) through the years radiologists have become aware of the fact that in a number of cases an apparent widening of the superior mediastinum is not secondary to an enlarged thymus but to artefacts related to the position of the patient, stage of inspiration, etc.; (2) not all thymic hyperplasias are accompanied by symptoms and, therefore, there is no need to treat such cases; (3) the usefulness of the adrenocorticosteroids in the treatment of this condition has been demonstrated; and (4) several papers have been published on the late appearance of carcinoma, particularly of the thyroid gland, in individuals previously treated by roentgen rays for thymic enlargement.

The authors review and discuss this topic as it is evaluated today, particularly in the light of the most recent information published in the American literature.

In relation to the roentgen diagnosis of thymic hyperplasia, the authors analyze the technical factors which not infrequently lead to the incorrect diagnosis of enlargement of the thymus, and the other pathologic conditions of the thymus which could be incorrectly interpreted as hyperplasia.

It is well known that in about 60 per cent of the cases an enlargement of the thymus does not produce any clinical symptoms. In these cases and in a few others in which symptomatology is minimal, there is no need for medical or roentgen therapy. The authors point out that the clinical picture, and not the roentgen findings, should determine whether to consider any treatment.

Several papers in recent medical literature deal with the use of adrenocorticosteroids. The immediate results obtained by the authors are very satisfactory but after some time the symptoms tend to reappear in a certain number of cases. To obtain a satisfactory result one must administer a dose of 5 mg. of ACTH, or 1.5–2 mg. per kilogram of prednisolone *per diem*. These dosages are not without danger and, in the authors' opinion, adrenocorticosteroid therapy in infants is rather hazardous, particularly, if the treatment is prolonged.

Over the past ten years, and almost exclusively in the American literature, several papers have pointed out the relationship between roentgen therapy for thymic hyperplasia and cancer of the thyroid. It seems to the authors, however, that one reason for this high incidence is the different technique of irradiation adopted in the United States, where rather large fields have been used. In European Departments of Radiotherapy the emphasis was and is on the use of very small fields, so that the thyroid gland cannot be included in the portal of entry of the radiation beam. Latourette and Hodges report a series in which there was only 1 case of thyroid carcinoma, and that in a patient who was irradiated through a large field. Similar conclusions on the importance of a small field were drawn by Conti *et al.* in 1960.

The authors conclude by recommending roentgen therapy for only those cases in which it is indicated after a complete evaluation of the clinical and roentgen findings. The importance of small fields is emphasized.—*A. F. Govoni, M.D.*

Mathé, G., Amiel, J.-L., and Bernard, Jean. Traitement de souris AkR à l'âge de six mois par irradiation totale suivie de transfusion de cellules hématopoiétiques allogéniques. Incidences respectives de la leucémie et du syndrome secondaire. (Treatment of AkR mice at the age of six months by total irradiation followed by transfusion of allogenic hematopoietic cells. Respective incidence of leukemia and the secondary syndrome.) *Bull Assoc. franç. de l'étude du cancer*, July–Sept., 1960, *47*, 331–340. (From Centre de Recherches de l'Association Claude-Bernard, Hôpital Saint-Louis, Paris, France.)

In this experiment, mice of the AkR strain showed spontaneous induction of leukemia. These mice were treated at the age of six months by a lethal dose of irradiation followed by a transfusion of myeloid cells of adult or fetal C_3H or $C_{57}Bl_6$. The control mice died of leukemia between the sixth and fourteenth months (median, eight months and eighteen days). The mice treated as above also died between the sixth and fourteenth months but the median age at death was seven months, thirteen days. Apparently these animals did not die of leukemia but, rather, died of the changes induced by the treatment. The secondary syndrome includes lymphoid aplasia, hyperplasia of pyroninophilic cells and necrotic changes in the liver and spleen.—*Charles M. Nice, Jr., M.D.*

Boyd, Elizabeth, Buchanan, W. Watson, and Lennox, Bernard. Damage to chromosomes by therapeutic doses of radioiodine. *Lancet*, 1961, *1*, 977–978. (From: Western Infirmary, Glasgow, Scotland.)

Last October, Tough, Buckton, Baikie and Court Brown reported that roentgen rays applied to the spine in the relatively heavy doses used in treatment of spondylitis ankylopoietica produced a shower of chromosomal abnormalities in cultures of the blood. This observation opens up the possibility of a biologic comparison of the effect on the marrow of different forms of irradiation. The authors point out that very little is known of the dose actually received by structures other than the thyroid, when radioiodine is administered in treatment dosage for the thyroid. It was decided to try to find out whether treatment with radioiodine had an effect on chromosomes similar to that of spinal irradiation.

Tough and associates noted a fall in the proportion of cells with the normal chromosome number, and the appearance of chromosomes with structural abnormalities. These structural changes consist of dicentric abnormalities and fragments. These are both extremely rare in nonirradiated cultures. The authors state that they have never seen a dicentric chromosome in any other material. They also believe that there is some indication that structural abnormalities appear later and persist longer than abnormalities in number. They feel that it is already justifiable to conclude that radioiodine can produce changes not very different in degree from those described by Tough and associates as following a single dose of 250 rads to the spine. These findings raise the question whether radioiodine therapy can cause leukemia. In a few reported cases leukemia has followed such treatment. Pochin made a very extensive survey of this treatment in thyrotoxicosis, and concluded that the incidence of leukemia could have been due to chance. However, the larger doses used for thyroid cancer metastases may well carry a more substantial risk, especially when they are repeated several times.

Six brief case reports of patients treated with radioiodine are included, with a chart of chromosome counts.—*Douglas S. Kellogg, M.D.*

Stewart, John S. S., and Sanderson, Ann R. Chromosomal aberration after diagnostic x-irradiation. *Lancet*, 1961, *1*, 978–979. (From: Department of Surgery, and Department of Zoology, Queen's College, Dundee, Scotland.)

Chromosome damage in man induced by therapeutic irradiation has recently been reported by Tough and associates. The authors have observed a similar type of chromosomal aberration in leukocyte culture of the peripheral blood from a patient with medullary dysgenesis (chromatin-positive Klinefelter's syndrome) shortly after exposure to diagnostic irradiation. The report of Tough and associates that dicentrics and other chromosome aberrations may be induced by therapeutic irradiation *in vivo* prompted the authors to recheck their data. It was recalled that the patient had been exposed to diagnostic roentgen rays before the blood sample was taken for culture.

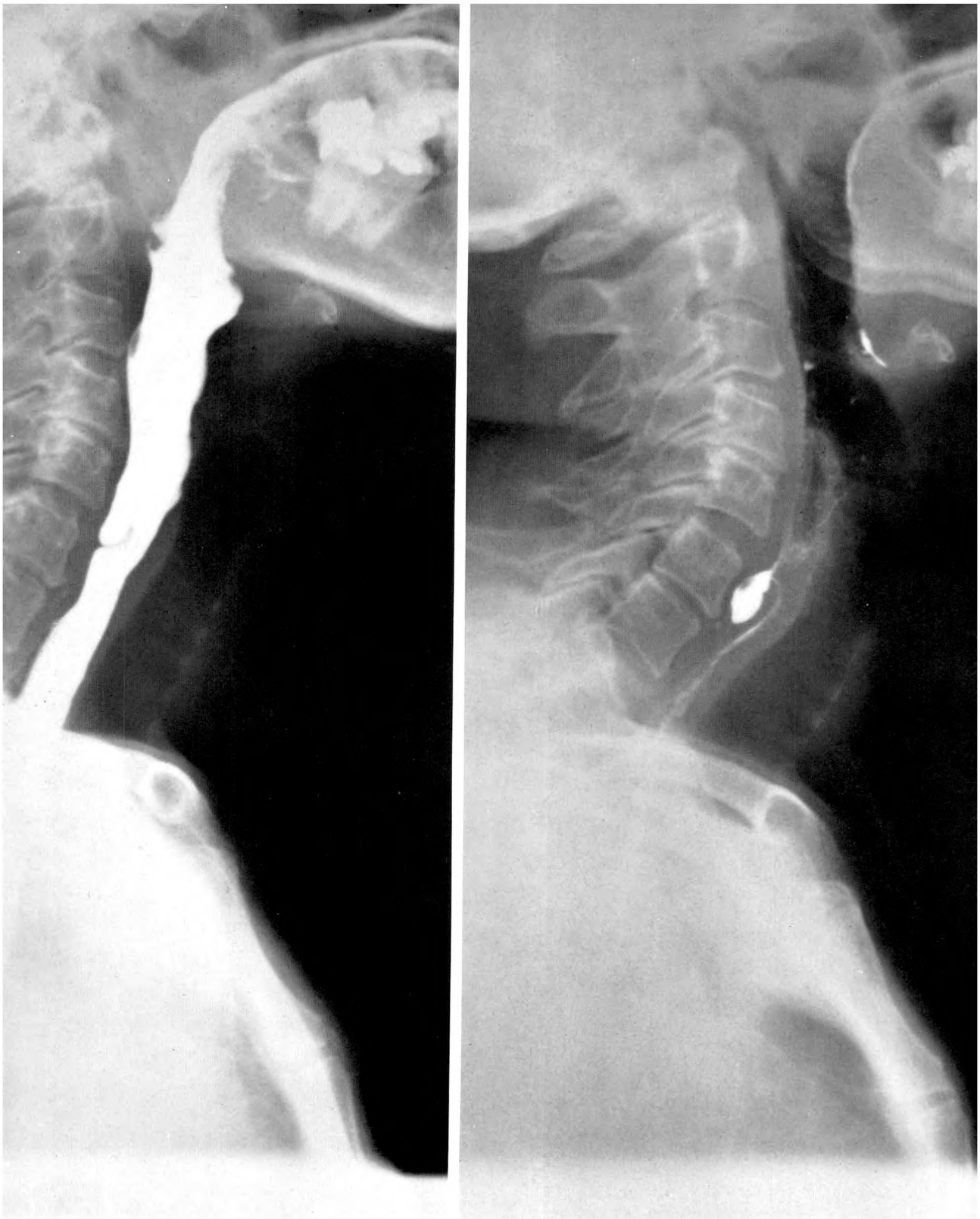
A blood sample was used to set up a culture of leukocytes, which was harvested three days later. Thirty-one plates of high technical quality were suitable for analysis. In 29 the sex chromosome constitution was XXY, and the chromosome number was 47. In the other two plates an abnormally long and apparently dicentric chromosome was present. The aberration might have been induced by the diagnostic irradiation *in vivo* or by background radiation. It is also possible that it might be related to patient's abnormal karyotype, or it could have arisen in culture. Further work is necessary to investigate these possibilities.—*Douglas S. Kellogg, M.D.*

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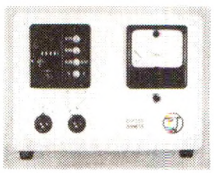
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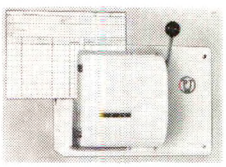
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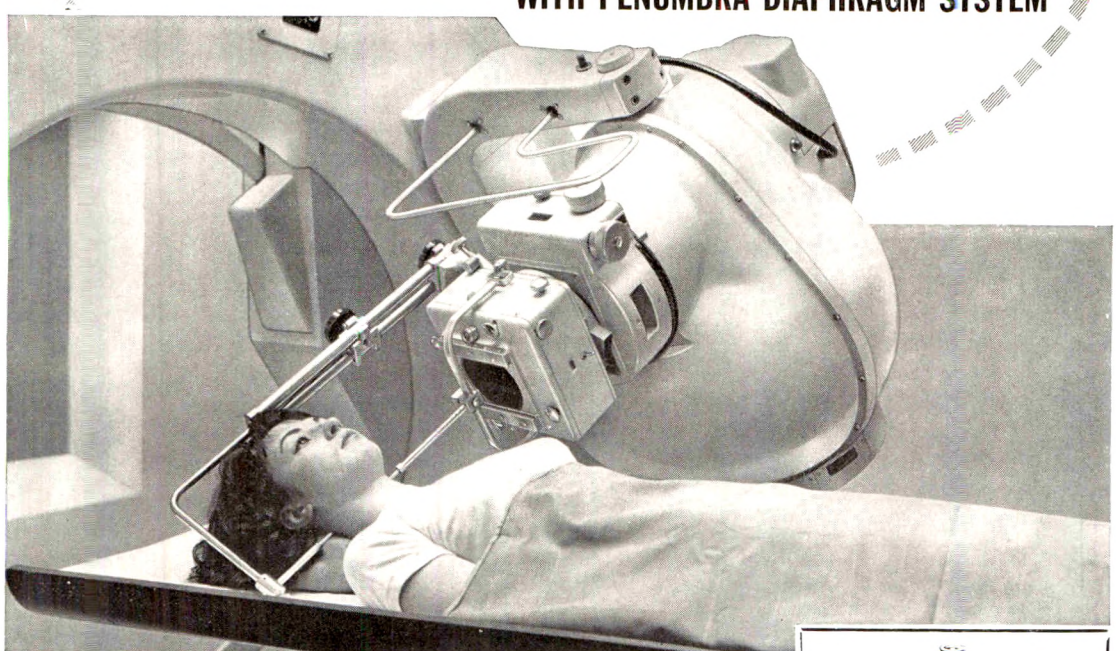
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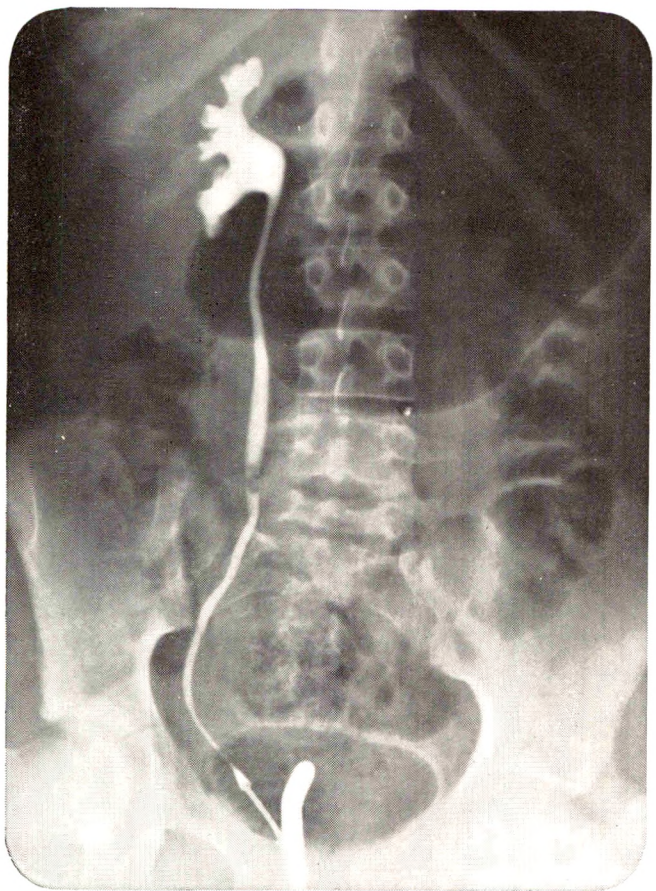


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THE PERFORMANCE OF SCREEN INTENSIFICATION AND CINEFLUOROGRAPHIC SYSTEMS*

By RUSSELL H. MORGAN, M.D.
BALTIMORE, MARYLAND

IT IS a great honor and privilege to speak to you today on the occasion of the Annual Oration of the Philadelphia Roentgen Ray Society. It is appropriate that this year's oration has been dedicated to the distinguished engineer, Mr. H. Clyde Snook. Technologic advancement in the field of Radiology has never been more rapid than in the last few years. Yet, such progress has been possible only with the sound physical and engineering foundation which men like Clyde Snook laid for Radiology during the early period following the discovery of the x-ray. His tireless efforts to develop and build apparatus which had practical usefulness to the radiologist opened the way for physicians everywhere to reap the enormous benefits of the x-ray.

I am indebted to Mr. Charles Smith and to Dr. Richard Chamberlain for much of the information I have to tell you about Mr. Snook. Dr. Herbert Stauffer has kindly given me valuable data as well.

HOMER CLYDE SNOOK: A HISTORICAL SKETCH

Homer Clyde Snook was born in 1878 in Antwerp, Ohio, the son of Wilson H. and Nancy Jane Snook. After the completion of his primary education in the public schools of that city, Snook became a student at Ohio Wesleyan University and received his A.B. degree there in 1900. At the time Röntgen made his discovery of the x-ray, Snook was a student of Professor W. G. Hormell in the university's Department of Physics. Because both were enormously interested in Röntgen's discovery, they at once began experimental work to produce x-rays in their laboratory. Following a period of several days of intense activity, activity which rarely has been paralleled, Snook and Hormell were successful in putting together a system which indeed generated x-rays.

Although Snook taught for a short time at Allegheny College after his graduation, much of his life was spent in Philadelphia. Snook's decision to move to this city was fortuitous for there is little doubt that much of his success came as a result of the environment provided by this outstanding center of Clinical Radiology. Snook not only had the opportunity to test his ideas with many of the world's finest radiologists, but of even greater importance he

* From the Department of Radiology, The Johns Hopkins University and Hospital.
Presented as the H. Clyde Snook Annual Oration at The Philadelphia Roentgen Ray Society, November 10, 1960.

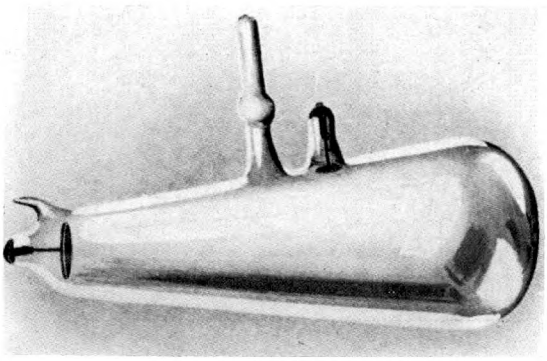


Fig. 1. The Hittorf tube.

received from these men a scientific stimulation seldom equaled anywhere.

The story of Snook is inseparable from the story of Radiology during the first two decades of this century. The source of the x-radiation which Röntgen discovered and which Snook soon duplicated in Ohio was a tube variously known at different times as the Geissler tube, the Plucker tube, the Hittorf tube, and the Crookes tube. All were essentially the same in basic design and were constructed for the study of the characteristics of electrical discharges in gases. These tubes had a cathode and an anode (Fig. 1). The anode, however, was in such a position that when the gas was ionized within the tube by the presence of a high potential across the two electrodes, electrons were projected from the cathode on the glass at the far end of the tube. The electron bombardment of the glass caused it to fluoresce with a green color. Although these tubes had been used as far back as 1859 by Plucker, it remained for Röntgen to discover that, in addition to green fluorescence, x-rays were also produced by the electron-glass interaction. Interestingly, at the time of Röntgen's discovery, the attention of more than one American physicist was being directed toward the inexplicable fogging of unopened packets of photographic plates placed in the neighborhood of a Crookes tube.

Professor Röntgen did not discover the x-ray by accident. As related in an anonymous account written for the Snook-Roentgen Manufacturing Company of Philadelphia in 1916, Sir James Mackenzie Davidson told Mr. Snook his recollections of an interview with Professor Röntgen in Würzburg shortly after the discovery of the rays. Sir James stated that he asked the question, "What were you doing with the Hittorf tube when you made your discovery?" "I was looking for invisible rays," replied Röntgen. "What made you use a barium platino-cyanide screen?" "In Germany we use it to reveal the invisible rays of the spectrum, and I thought it a suitable substance to detect any invisible rays the tube might give off." The sudden shining of that screen led to one of the greatest scientific discoveries of history.

In the twenty to thirty years following the discovery of the x-ray, Snook played a vital role in technologic developments in the United States. Although he is known for many things, Snook's greatest contribution undoubtedly was the so-called interrupterless x-ray transformer shown in Figure 2. For the first dozen years after the discovery of the x-ray, roentgenologists and physicists employed induction coils (Fig. 3) and static machines (Fig. 4) to develop the electrical potentials needed to produce x-rays. These instruments, however, had many disadvantages including the limited power which could be delivered to the x-ray system.

It was at this stage of the development

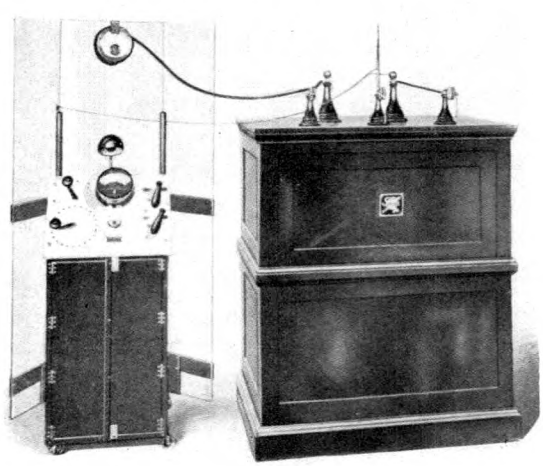


Fig. 2. The Snook interrupterless x-ray transformer.

of x-ray apparatus that Snook, together with his colleagues Herbert White and Edwin Kelley, organized the Radioelectric Company which a few months later became the Roentgen Manufacturing Company. Their first office and workshop was a second story back room at 226 Ionic Street, Philadelphia (Fig. 5). These modest quarters, which were in one of the oldest sections of Philadelphia, were destined to be the birthplace of Snook's major contribution to Radiology.

In endeavoring to find some means to prevent the inverse current from passing through an x-ray tube, Snook made a thorough analysis of the erratic performance of the induction coil by taking oscillographic readings of a coil of the Ruhmkorff type in the Randal Morgan Laboratory of Physics at the University of Pennsylvania. His report, published in January, 1907, was the first comprehensive study of the vagaries of this type of apparatus. During his investigations he devised a high-tension synchronous spark gap and from the oscillographic readings made with this apparatus conceived the idea of using rectified alternating current for exciting the x-ray tube. His first step was to replace the induction coil with a closed core transformer, after which he developed the rotating rectifying switch which became so closely identified with his name.

The experimental design and early production of the interrupterless transformer

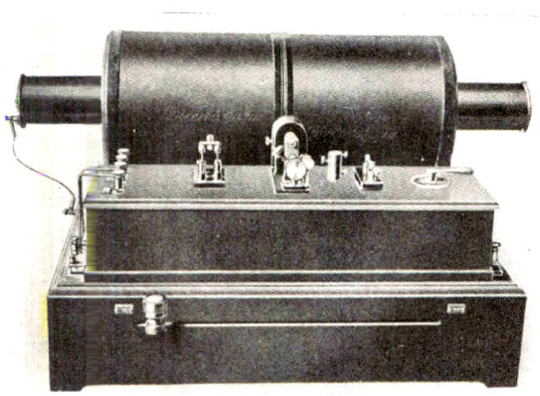


Fig. 3. The Queen induction coil.

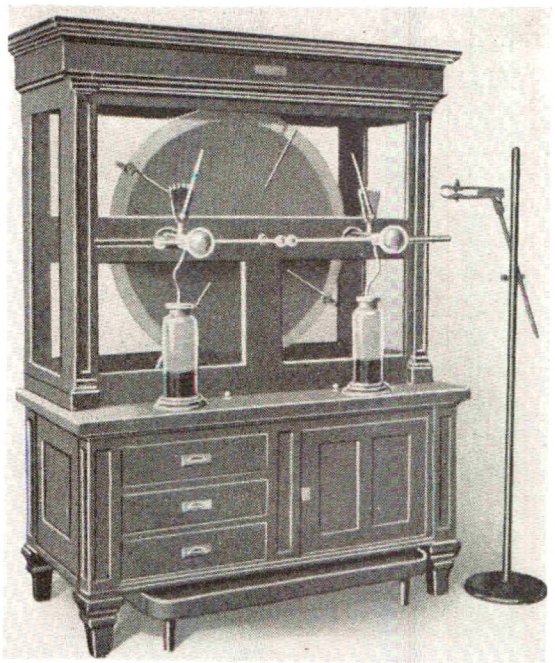


Fig. 4. A typical static machine used in the generation of x-ray tube potentials early in this century.

was done in the little back room on Ionic Street and the first unit for hospital use was installed in the Jefferson Hospital in Philadelphia in June of 1907. After this time there followed a rapid replacement of the induction coil with the transformer. In 1908 Mr. Snook described his machine in a paper given before the International Roentgen Congress in Amsterdam. He also visited England and Germany and after that time for a number of years the interrupterless transformer was manufactured widely throughout the world.

It may be worth recording that one of the earliest transformers manufactured by Snook was sold to Baetjer at The Johns Hopkins Hospital in 1907. Historians of this conservative institution in Baltimore may someday comment on the fact that this equipment was still in operation, carrying a heavy clinical load, as late as 1946.

Snook played an important role in radiologic developments in Philadelphia. He was among the founders of the Philadelphia Roentgen Ray Society and was active in its affairs until he moved from Philadel-

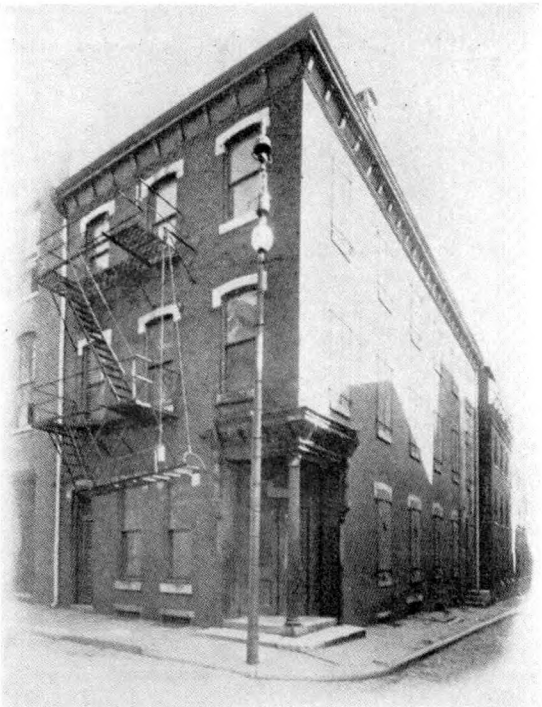


Fig. 5. The birthplace of the interrupterless transformer, 226 Ionic Street, Philadelphia, Pennsylvania.

phia in 1916. Following his departure from Philadelphia, Snook became Vice-President of the Victor Electric Company of Chicago. From 1918 to 1925 he was a member of the engineering staff of the Western Electric Company. In 1925 he joined the Bell Telephone Laboratories and in 1927 he became an independent consulting engineer.

Snook was a Fellow of the American Institute of Electrical Engineers and of the American Physical Society, and a member of the American Roentgen Ray Society. He was also the recipient of many honors, including the Edward Longstreth Medal of the Franklin Institute in 1919, the Gold Medal of the Radiological Society of North America in 1923 and the Gold Medal of the American College of Radiology in 1928. He was honored by his alma mater in 1926, when he was granted a degree of Doctor of Science. H. Clyde Snook died in Summit, New Jersey, September 22, 1942.

The world owes much to Clyde Snook. He brought distinction to his profession. Although the march of progress now has left Snook and his contemporaries far behind, we should not forget the contributions made by these dedicated men, for without them we should not be where we are today.

PRINCIPLES OF SCREEN INTENSIFICATION

I should like to turn now to the field of screen intensification and cinefluorography, two areas in which Snook undoubtedly would have been intensely interested if he were still alive. In my discussion of these subjects I should like to speak first of screen intensification and to refer briefly to a number of the fundamental principles upon which it is based. Such a discussion is necessary as a prelude to my comments on cinefluorography, since without screen intensification cinefluorography would have little more than theoretic interest to the radiologist due to the excessively large radiation doses which must be used when non-intensified techniques are employed.

When the useful beam of an x-ray is projected through an anatomic or other structure, many and some times most of the photons which comprise the beam are absorbed. A few, however, pass through the structure to emerge on the other side. If these are allowed to fall on a fluorescent screen, some are absorbed and their energy is converted into light.

If all anatomic tissues absorbed x-ray photons equally, the number received by the fluoroscopic screen would be uniform from one portion of the screen to another and, hence, the light generated by the screen would exhibit no image pattern. If, on the other hand, some tissues absorbed more x-ray photons than others, the brightness of the screen would not be constant from one point to another but instead would vary in accordance with the configurations of the anatomic structures through which the radiation passes; that is, the screen would bear an image pattern. Although many tissues absorb x-rays nearly equally,

others, because of differences in density and/or atomic number do not. Therefore, the images of many anatomic components may be recorded fluoroscopically and roentgenographically.

From the description of the manner in which fluoroscopic images are produced, it will be clear that the diagnostic information recorded by a fluoroscopic screen is carried from patient to screen by the myriads of x-ray photons which comprise the x-ray beam. Indeed, each transmitted photon carries a certain small increment of diagnostic information and it is the sum of all of these bits of data which governs the total quantity of diagnostic information recorded by the screen at any instant. The amount of information provided by a screen can never be greater than that carried by the photons which impinge upon it. It, of course, can be less if such factors as fluoroscopic grain size do not permit efficient utilization of the information carried by the photons. The point that must be emphasized, however, is that the diagnostic information provided by a fluoroscopic screen can be no greater than the sum of all of the increments of information carried to the screen by the photons of the x-ray beam. What has been said for the fluoroscopic process is also valid, of course, for roentgenography and for cinefluorography.

Since each x-ray photon may be assumed to have associated with it a certain amount of diagnostic information, it follows that when an x-ray beam of high radiant intensity is projected through a patient, the detail recorded on a fluoroscopic screen will be considerably greater than when a beam of low intensity is used. In the first instance, there are a great many x-ray photons carrying diagnostic information and hence the detail of the resultant image is relatively good; in the second instance, the number of x-ray photons is smaller and hence less diagnostic information is available and degradation of image quality results. That this is true may be easily demonstrated if one fluoroscopes a patient first with an x-ray tube current of 5 ma. and then with a current of 0.5 ma., all other factors being equal in the two situations. Fluoroscopic image detail will be observed to be substantially greater when the higher x-ray tube current is used.

The foregoing discussion provides a qualitative understanding of the fluoroscopic process. For a quantitative evaluation of fluoroscopic performance, it is necessary that we turn our attention to the quantum statistics of physiologic optics.

It has been shown by physiologic experiment[4] that the performance of the eye measured in terms of its ability to record visual data is largely limited by statistical fluctuation in the number of light photons reaching the retina. Although most individuals are unaware that such fluctuation exists, it nevertheless is present to a greater or lesser degree under all viewing conditions and ultimately determines the fineness of structure that the eye can perceive. Fluctuation of course does not constitute the only factor which limits visual performance. In diagnostic radiology, such factors as the diameters of the retinal rods and cones and a large number of physical factors associated with the x-ray equipment and recording media also introduce limitations. However, these factors only contract the limits already set by statistical theory and hence are of secondary importance in a discussion where the fundamentals of data recording are under examination.

In general, the statistical fluctuation in light intensity which occurs at the retina of one's eye is proportional to the square root of the average number of photons projected on the retina within the storage time of the eye (about 0.2 second). For example, if the eye is observing an object 1 mm. in diameter at a viewing distance of 20 cm., the number of photons reaching the retina from the object during each 0.2 second will be of the order of one million at normal levels of illumination. Therefore, the average fluctuation in light intensity at the retina from moment to moment will be approximately the square root of one million; that is, the fluctuation will be of the

order of ±1,000 photons or about ±0.1 per cent of the average light intensity. Now, if the illumination of the object is reduced to levels comparable to those occurring at fluoroscopy, the effective number of photons reaching the retina within 0.2 second may be as small as 100. Accordingly, such a number will have an associated average fluctuation of ±10 photons or ±10 per cent of the average light intensity. Hence, when the illumination of an object is reduced, the per cent fluctuation in the rate at which photons arrive at the retina increases.

The effect of this fluctuation will be evident if one considers the situation which occurs when the 1 mm. object under observation is surrounded by a field whose average illumination is 5 per cent greater than that of the object; that is, the contrast between the object and the surrounding field is 5 per cent. Under such a condition, if the object is observed under normal illumination, where the fluctuation in brightness from moment to moment is ±0.1 per cent, the fluctuation will not interfere noticeably with the perception of the object. On the other hand, if the illumination of the object is at a level corresponding to that occurring in fluoroscopy where the fluctuation is of the order of ±10 per cent, the object may at one moment appear darker and at the next moment lighter than the surrounding field. Obviously, such variation will interfere markedly with the perception of the object and will create considerable confusion in the mind of the observer.

The magnitude of the statistical fluctuation which occurs from moment to moment in the number of photons received by the eye of an observer during fluoroscopy and the extent to which such fluctuations quantitatively affect image perception have been the subject of exhaustive study.[5] It has been found that the magnitude of the fluctuation is largely governed by that stage of the fluoroscopic process where the photon intensity (*i.e.*, the number of photons per unit area per second) falls to its lowest level and that the limits set by this fluctuation on the size of the smallest image which an observer can detect is given by the formula:

$$d = \frac{5}{C(nt)^{1/2}} \times 10^2 \qquad (1)$$

where d is the diameter of the smallest perceptible image in millimeters, C is the per cent contrast of the image, t is the storage time of the eye in fluoroscopy or the exposure time of the film in cinefluorography and n is the number of photons per second emerging from each square millimeter of the image during that stage of the fluoroscopic or cinefluorographic process when the photon intensity falls to its lowest level.

Figure 6 is a graphic presentation of the photon intensities which exist during the several stages of the fluoroscopic process. Stage 1 is a plot of the x-ray photon intensity prior to the beam's absorption by

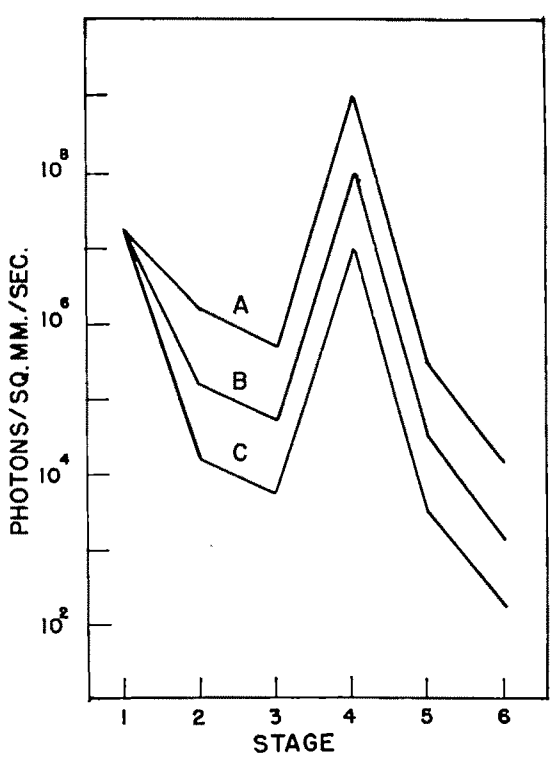


FIG. 6. Quantum diagram of the conventional fluoroscopic process during the examination of: A, the anteroposterior chest; B, the anteroposterior abdomen; and C, the lateral lumbar spine.

the patient under examination. The data are for a fluoroscope operating at 90 kvp., and 3 ma., with 3 mm. of aluminum filtration and a tube-screen distance of 27 inches. Stage 2 plots the photon intensity after the beam's absorption by A, a typical adult anteroposterior chest projection; B, a typical adult anteroposterior abdomen projection and C, a typical adult lateral lumbar spine projection. Stage 3 is a plot of the photon intensity absorbed by the fluoroscopic screen; Stage 4, the light photon intensity emitted by the screen; Stage 5, the number of light photons per second emitted by 1 sq. mm. of screen surface and admitted by the pupil of the eye when the viewing distance is 20 cm.; and Stage 6, the number of these photons which after admission to the eye, stimulate the retina.

It will be observed that the stage at which the number of photons per square millimeter per second reaches its lowest level is Stage 6, the stage at which photons are admitted to and stimulate the retina. When the data for Stage 6 are substituted in equation (1), the minimum perceptible images which can be seen at various levels of contrast for the three fluoroscopic projections under consideration may be easily calculated. The results of such calculations are shown in the dotted curves of Figure 7. The solid curves represent measured values of visual performance made on normal subjects. The ability of quantum statistics to describe the performance characteristics of the eye is apparent.

It will be observed from a perusal of Figure 6 that, if a screen intensifier with a photon intensification of 40 or more times were introduced between Stage 4 and Stage 5 of the fluoroscopic process, the stage at which the photon intensity reaches its lowest level would no longer be Stage 6 but instead would be that at which x-ray photons are absorbed by the fluoroscopic screen (*i.e.*, Stage 3). Under these circumstances, the quantum diagram for the anteroposterior chest projection would be that shown in the *solid* curve of Figure 8. Again,

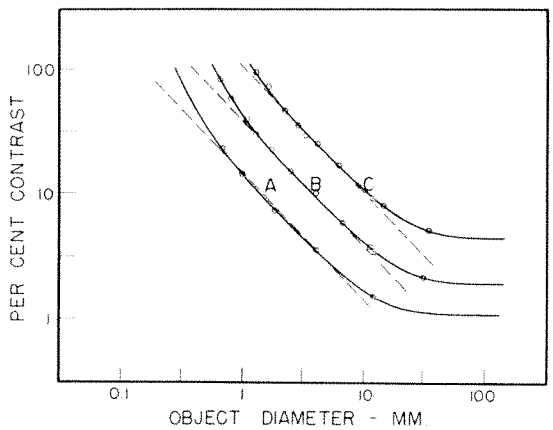


Fig. 7. Relationship existing between the diameter of the minimum perceptible image and image contrast during: A, anteroposterior chest fluoroscopy; B, anteroposterior abdominal fluoroscopy; and C, lateral lumbar spine fluoroscopy. Dotted curves represent values calculated from quantum statistics. Solid curves represent measured values of visual performance in normal subjects.

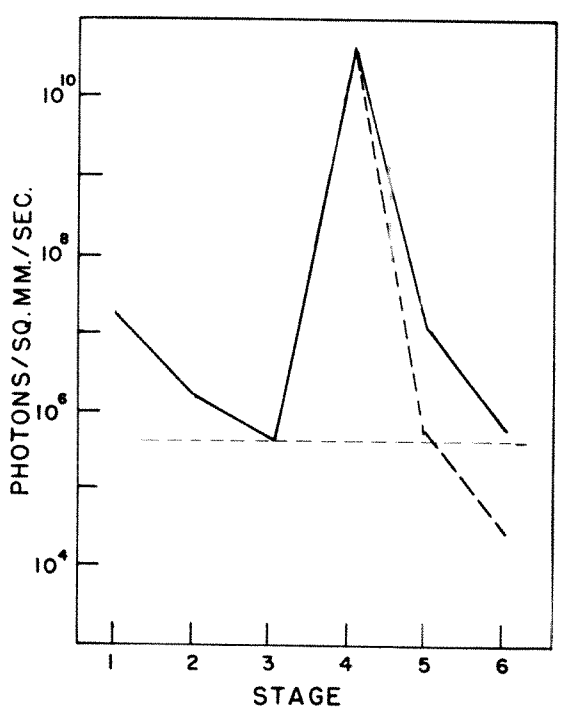


Fig. 8. Quantum diagram of the fluoroscopic processes when aided by screen intensification. Solid curve indicates data for a viewing distance equivalent to 20 cm. Dotted curve indicates data when viewing distance is equivalent to 100 cm.

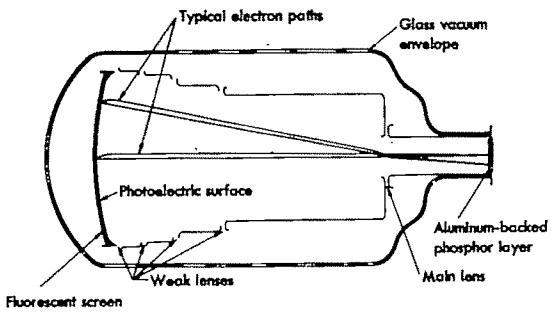


FIG. 9. X-ray screen intensifier of image amplifier type.

the data assume a viewing distance of 20 cm. It will be seen that, with the screen intensifier, the lowest level to which the quantum diagram descends is considerably higher than that when an intensifier is not employed. A considerable improvement may therefore be expected in the fineness of structure which may be perceived when such a device is used. Indeed, from Figure 8 and equation (1), the improvement should be of the order of 6 diameters.

IMAGE AMPLIFIERS

The most widely used type of screen intensifier is the electronic image tube or image amplifier,[1,8] an instrument which is shown schematically in Figure 9. This device consists of an evacuated glass envelope, at one end of which is an x-ray fluorescent screen located so as to intercept the x-ray photons emerging from the structure under examination; it is similar to the screens used in conventional fluoroscopy. A thin photoelectric layer is mounted on the screen's internal surface.

At the other end of the tube is a second fluorescent surface, whose diameter usually is only a small fraction of that of the first. This surface serves as a viewing screen and is backed with a thin aluminum layer to prevent its light from reaching the photoelectric surface at the other end of the tube. Between the two ends of the tube are placed a number of cylindrical electrodes which serve as electron lenses when suitable potentials are applied to them. Such an intensifier operates in the following manner: radiation from a conventional x-ray tube is projected through the structure under examination and is allowed to impinge on the tube's input fluorescent screen. In response to the light generated by this screen, the photoelectric layer emits electrons having a spatial distribution proportional to the brightness of the screen; that is, the fluorescent screen converts the x-ray image into a light image whereupon the photoelectric layer creates a corresponding electron image. Electrons from the photoelectric layer are accelerated through the length of the tube under the influence of the electrical potentials applied to the cylindrical electrodes and fall on the viewing screen at the tube's distant end. The impingement of electrons on this screen produces a visible image which duplicates the pattern of the x-ray fluorescent screen. However, due to the acceleration of the electrons within the tube, the brightness of the viewing screen is many times greater than that of the x-ray screen. The brightness is further enhanced by the fact that the size of the former is small compared to that of the latter. The observer views the intensified image by means of an eyepiece or other optical system to bring the image back to normal perspective. In most screen intensifiers of the electron image type, the intensification ranges from 500 to 3,000 times. Of this, however, from 30 to 100 times is the result of the minification of the image. Only 25 to 50 times is due to an actual increase in the number of light photons.

The improvement in fluoroscopic vision obtainable with intensifiers of the image amplifier type approaches the theoretic levels predicted by the data of Figure 8 if a viewing distance is used in which the visual field subtends the same angle to the eye as that when a conventional fluoroscope is viewed at a distance of 20 cm. Unfortunately, however, image amplifiers to be clinically practical require that the optical system place the viewer at an equivalent position substantially greater than 20 cm. from the screen. Indeed,

equivalent viewing distances in excess of 1 m. must be employed. Under these circumstances, the number of light photons admitted to the eye is substantially reduced, the performance of the intensifier is therefore degraded, and the quantum diagram of the fluoroscopic process assumes the pattern shown by the *dotted* curve in Figure 8. It will be seen that in this case the stage of the fluoroscopic process at which the number of photons per unit area per second reaches its lowest level is that at which photons are admitted to and stimulate the retina. Also, the quantitative level of this stage is not much greater than that of the similar stage in conventional fluoroscopy. Hence, image amplifiers when viewed with currently available optics do not yield a clarity which is much improved over that of conventional fluoroscopy. Of course there is a great advantage to screen intensification in its elimination of the need for dark adaptation. However, the full potential of screen intensification from the standpoint of its resolution or clarity has not been achieved.

Some improvement in the performance of image amplifiers has been made through their combination with television systems. With these systems the viewing conditions may be made sufficiently more satisfactory so that the resolution often is increased by a factor of 2. The contrast enhancement provided by television systems also improves the performance of screen intensifiers at low contrast levels.

SOLID STATE AMPLIFIERS

Although the image tube is, by all odds, the most widely used type of screen intensifier at the present time, several other varieties have been proposed. Some of these are not likely to find wide application, principally because they do little to increase the efficiency with which x-ray photons are utilized. One system,[2] however, which exhibits some promise is that shown in Figure 10. The system consists of two principal elements: a photoconductive layer which intercepts the x-ray photons coming from the structure under examination and an electroluminescent layer which emits light when it is placed in an alternating electric field. The two layers are separated by a thin film of opaque material of high electrical resistance. Also, a thin plate of conducting glass and a thin sheet of electrically conductive material such as aluminum are applied to the free surfaces of the electroluminescent and photoconductive layers, respectively. When the system is exposed to x-rays and a sinusoidal potential is applied to the aluminum and glass electrodes, a fluoroscent image of the structure under examination appears on the screen.

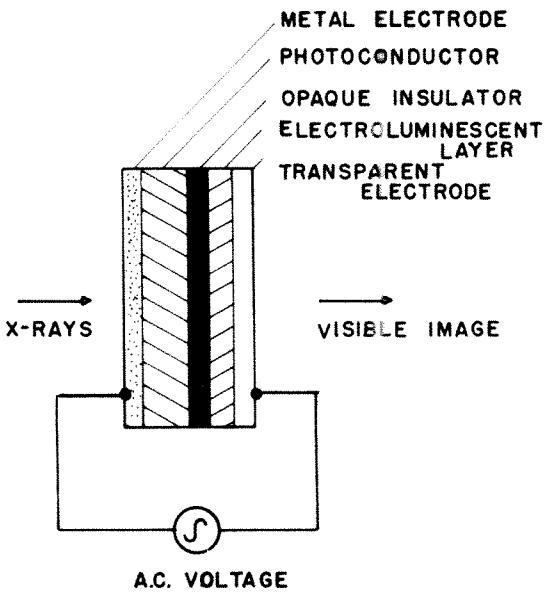


FIG. 10. Solid state screen intensifier.

The principles of operation are as follows: When x-rays are absorbed by the photoconductive layer, the layer's electrical resistance decreases and hence a greater fraction of the potential which prevails between the aluminum and glass electrodes appears across the electroluminescent layer. As a result, this layer emits light which may be seen by the observer through the glass electrode. Since the resistance of the photoconductive layer varies from place to place in accordance with the radiant intensity of the various x-ray images impressed

upon it, the electroluminescent layer will exhibit a series of images which conform to the x-ray pattern.

Many variations of the photoconductive, electroluminescent panel have been proposed and experimental models constructed. Although such panels are capable of producing light outputs which are several times those of conventional fluoroscopic screens, their response is unfortunately so slow that they are almost useless as fluoroscopic devices. Images smear badly when any motion is present. It appears that this characteristic is due to the rather poor mobility of the charges within the photoconductive and electroluminescent layers. Although it may be anticipated that this problem will eventually be overcome, this type of screen intensifier is not yet suitable for fluoroscopic work.

CINEFLUOROGRAPHY

As indicated earlier, screen intensifiers of the image amplifier type are proving of great value in cinefluorography. Indeed, without such instruments practical cinefluorography would not be possible because of the excessive radiation doses required when conventional fluoroscopic screens are photographed. The gains in illumination made possible by screen intensifiers have changed this situation entirely. In fact, when an electron image tube is used with a television system to increase the intensification still further, it is possible to make x-ray motion pictures with the use of no more radiation than that employed in fluoroscopy, even during the cinefluorography of dense abdominal structures.

In recent years, considerable controversy has arisen concerning the techniques best adapted for cinefluorography. Should one record directly from the image tube? Does recording from a television monitor provide the greatest number of advantages? Should one use 16 mm. film or 35 mm. film? There are many advocates of each technique, each group being certain that its method of operation is the preferable one. It is not surprising, then, that often those who plan to enter the field of cinefluorography become confused by the various claims and counterclaims. Unfortunately, most of the tenaciously held opinions are based upon limited experience where critical comparative experiments have not been carried out.

In spite of the confusion which exists within the field of cinefluorographic technology, experimental data are now at hand which substantially clarify the picture. These data show that, although the type of motion picture equipment employed in cinefluorography has some influence upon the clarity of reproduction, another factor is of more fundamental importance. This factor is the exposure dose rate applied to the patient during cinefluorography. Regardless of the equipment used, if the exposure dose rate is low, image quality will be poor. When the exposure dose rate is increased, image quality improves. The reason for this is well illustrated in the quantum diagram in Figure 11 where the photon

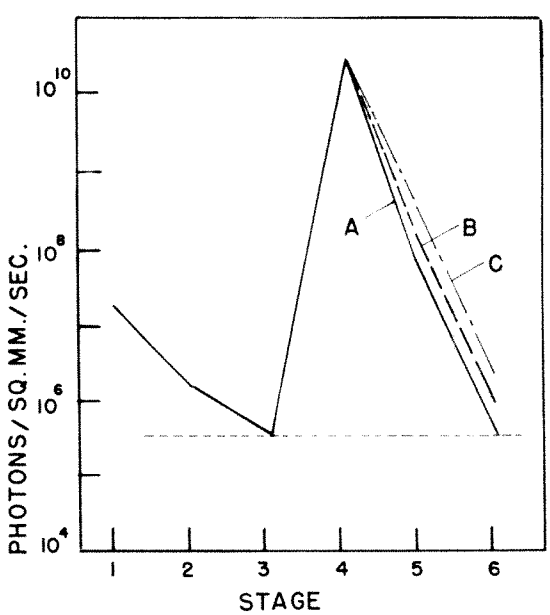


FIG. 11. Quantum diagram of the cinefluorographic process. Data apply to a typical anteroposterior chest examination performed with a 9 inch image amplifier with an intensification of 3,000. Curve A, 16 mm. film and f/1.5 camera lens; curve B, 16 mm. film and f/1.0 lens; and curve C, 35 mm. film and f/1.5 lens.

intensity prevailing at the various stages of the cinefluorographic process is plotted for a typical anteroposterior chest cinefluorographic examination when a 9 inch image amplifier, having an intensification of 3,000, is employed. Stage 1 indicates the x-ray photon intensity (*i.e.*, the number of x-ray photons per square millimeter per second) prior to the absorption of the beam by the patient when the x-ray machine is operating at 90 kvp. and 10 ma. with 3 mm. aluminum filtration, a tube-screen distance of 27 inches and a cinefluorographic frame rate of 60 frames per second. Stage 2 indicates the photon intensity after absorption of the beam by the chest; Stage 3, the photon intensity absorbed by the input screen of the image amplifier; Stage 4, the number of light photons generated at the output screen by the photon intensity of Stage 3; Stage 5, the number of light photons admitted to the film by the optical system of the cinefluorographic camera by the photon intensity of Stage 3; and Stage 6, the number of photographic grains produced in the developed motion picture film by the photon intensity of Stage 3. Curve A represents conditions for 16 mm. cinefluorography in which an f/1.5 camera lens is employed. Curve B is for the same circumstances as Curve A except that an f/1.0 optical system is used. Curve C is for 35 mm. cinefluorography with an f/1.5 optical system.

It will be observed that in all cases, the stage at which the number of x-ray photons per unit area per second reaches its lowest level is the stage at which x-ray photons are absorbed by the intensifier (Stage 3) and not the stage at which x-ray images are recorded on motion picture film. Consequently, from quantum statistics, cinefluorographic detail under the conditions set forth in Figure 11 is not dependent on the type of film used but on the exposure dose rate prevailing at the input screen of the intensification system.

From a perusal of Figure 11, it will be apparent that, if the intensification of the image amplifier becomes less and/or the f/number of the camera lens is made greater, the performance of the cinefluorographic process ultimately deteriorates and becomes a function of the size of the recording film, since under these circumstances the stage of lowest photon intensity shifts to that at which film recording takes place. The deterioration first affects 16 mm. recording and for a given lens aperture is greater for 16 mm. film than for 35 mm. materials. However, as stated in foregoing paragraphs, when the lowest level of photon intensity occurs at the stage when the image amplifier's input screen absorbs x-rays, the type of film has very little to do with image quality. The circumstances under which this condition is satisfied is expressed by the formula:

$$\frac{TcaF}{4f^2m^2} \geq 1 \qquad (2)$$

where c is the number of light photons emitted by the input screen of the image amplifier per x-ray photon absorbed, a is the intensification factor of the image amplifier, T is the fractional transmission of the optical system, f is the effective f/number of the optical system, m is the minification of the cinefluorographic image in respect to the image appearing on the input phosphor of the amplifier, and F is the fractional efficiency of the photographic emulsion. Typical values for T, c, and F are 0.4, 2,000 and .005, respectively. The equation therefore reduces to:

$$\frac{a}{m^2f^2} \geq 1 \qquad (2a)$$

Values of m for 5 and 9 inch amplifiers and for 16 and 35 mm. film are given in Table 1.

Equation (2) is of fundamental importance in cinefluorographic design. It indicates when a 35 mm. camera is to be preferred to a 16 mm. unit; more important, it permits one to determine the conditions under which maximum image quality may be determined regardless of film size. For example, if one wishes to record from a 9 inch intensifier with a 16 mm. camera under

TABLE I

MINIFICATION VALUES FOR 16 MM. AND 35 MM. CINEFLUOROGRAPHY MADE FROM 5 and 9 INCH IMAGE AMPLIFIERS

Film	Image Amplifier	
	5 inch	9 inch
16 mm.	17	30
35 mm.	7	12.5

conditions when image quality will not deteriorate because of film size, equation (2) indicates that a lens having an aperture approaching f/1.0 must be used.

Equation (2) is also valid for cinefluorographic systems in which the recording is taken from a television monitor. Because of the higher intensification values these systems provide, one may employ relatively large f/numbers in the camera optics and still obtain maximal results with 16 mm. film. Indeed, the intensification factors are typically so large that 35 mm. film is quite unnecessary in this service.

The importance of the exposure dose rate prevailing at the input screen of the image amplifier in determining the quality of the cinefluorographic film is well shown in a practical manner in Figure 12. These films were made with a motion picture camera recording the information provided by an image amplifier equipped with an image orthicon television system. Frame A illustrates a view of the television monitor with an exposure dose rate at the input screen of the image intensifier of 500 μr per frame (the exposure dose per frame prevailing during cinefluorography of the chest with the motion picture camera operating at 60 frames per second and the x-ray equipment operating at 90 kvp. and 10 ma., with 3 mm. aluminum filter and a 27 inch

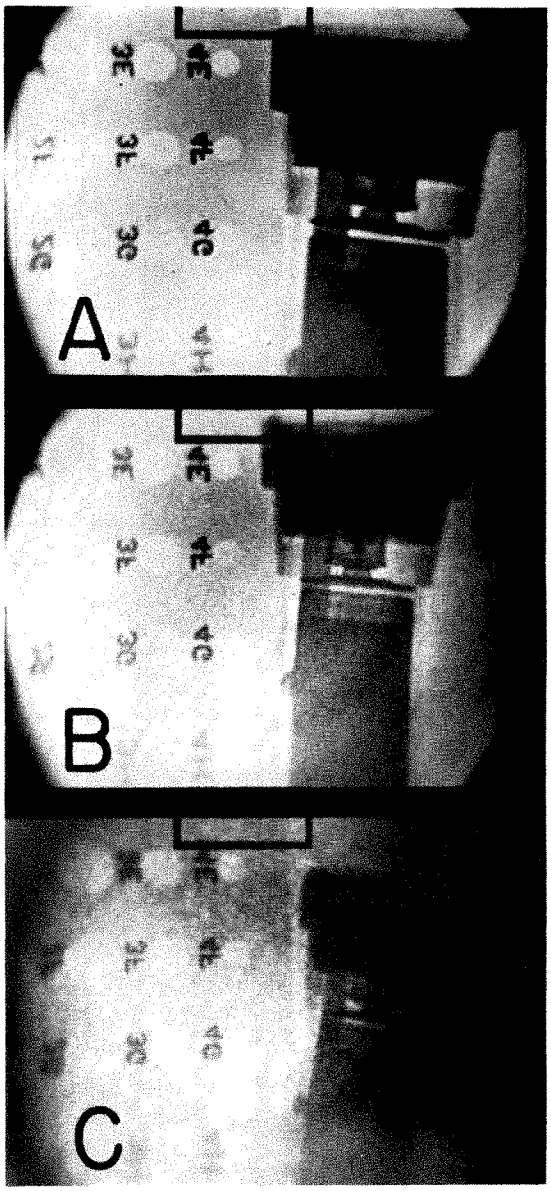


FIG. 12. Demonstration of the effect of exposure dose rate on cinefluorographic quality. Films were made from the television monitor of an intensifier consisting of a 9 inch image amplifier and an image orthicon television system. Frame A, single cinefluorogram with x-ray beam turned on at exposure dose rate of 500 μr per frame; frames B and C, same as frame A but with exposure dose rates of 50 and 5 μr per frame, respectively. Objects being roentgenographed were, on the left, a lucite plate with holes of varying size and contrast and, on the right, a flashlight. Note frank deterioration of image quality with decreasing exposure dose rate. Same cinefluorographic film, lens, and frame rate were used for all pictures. Compensation for de-

creasing screen brightness with decreasing exposure dose rate from frame to frame was provided by an increase in aperture of the lens between the image tube and image orthicon.

tube-intensifier distance). Frame B is the same as A but with the exposure dose rate per frame reduced to 50 μr. Frame C is the same as A but with an exposure dose rate per frame of only 5 μr. Although all films were made with the same motion picture film and with the television equipment performing under identical conditions, the influence of exposure dose rate on image quality is obvious. As the exposure dose rate decreases, the graininess visible in the picture becomes greater and the detail diminishes.

Since exposure dose rate values play a primary role in the determination of cinefluorographic quality, the question arises as to what cinefluorographic technique is best to employ under most circumstances. Usually, the convenience of 16 mm. film makes this material preferable to 35 mm. film, particularly if one has available intensification and optical systems adequate to make image quality independent of film size. In the case where motion picture films are recorded from a television monitor, there is no advantage in the larger film.

The choice between direct and television recording is more difficult. The maximum resolution of a 9 inch image intensifier is of the order of 0.25 mm.; that of an image amplifier equipped with an image orthicon television system is approximately 0.4 mm. Hence, direct recording produces somewhat greater detail at high exposure dose rates and with images of high contrast. Also, television recording is limited to frame rates of 30 frames per second and lower unless special equipment is used. Hence, this technique will usually not be suitable for many cardiac examinations where frame rates of 60 frames and over are desired. On the other hand, if a frame rate of 30 frames per second is adequate, television recording has many advantages. One of these is the increased intensification provided by television systems. As a result, abdominal cinefluorography of adults may be performed without excessive exposure dose rates. Another advantage is one's ability to change at will the intensification factor of a cinefluorographic system to meet the resolution requirements of the procedures to be recorded. The television method also has the advantage that it dissociates fluoroscopic and cinefluorographic operations. Hence, fluoroscopy can be conducted jointly with cinefluorography without one's having to discontinue one technique and start the other. This is particularly worthwhile in cinefluorography of rapidly changing events, such as those which occur in the pharynx during swallowing.

With the experience gained by many workers over the past few years, it is reasonably certain that cinefluography will play an ever increasing role in the field of diagnostic radiology. Even such techniques as myelography can be recorded by the cinefluorographic camera without excessive exposure of the patient. It is confidently anticipated that the next ten years will bring many advances in the diagnosis of disease by cinefluorography. Instruments capable of approaching the ideal in terms of performance are available. Their breadth of application only awaits the time needed to fully explore their potential.

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NORMAL ROENTGENOGRAPHIC ANATOMY OF THE HUMAN CIRCLE OF WILLIS*

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ROENTGENOGRAPHIC studies of the arterial system of the human brain are common. Methods of cerebral angiography in current use under normal circumstances opacify only isolated portions of the intracranial circulation. Usually, the posterior segment or the homolateral half of the anterior segment of the circle of Willis is visualized. Under these circumstances anatomic relationships of this important vascular complex must be inferred from a number of different angiographic studies. Such conditions make it exceedingly difficult to form valid estimates of normal anatomy in the circle of Willis or to judge the effects of health or disease upon it. Yet this arterial interchange is the structural distribution system which monitors regional cerebral arterial flow—and it is precisely in the field of disturbed *regional* flow that cerebrovascular disease exerts its effects. A reliable method of cerebral angiography which would produce simultaneous physiologic opacification of several or all anatomic parts of the circle of Willis might be expected to throw considerable light on normal hemodynamics in this little understood complex, and aid in evaluation of the effects upon cerebral circulation of disease or developmental deviation.

Once the feasibility had been established of routinely filling the drainage systems of carotid and vertebral arteries by retrograde brachial injection,[2] the submentovertical projection was added to the standard anteroposterior and lateral series for more complete angiographic survey of each patient. It was immediately discovered that in this view components of the circle of Willis in part, or in their entirety, were visualized with considerable clarity. The attainment of this objective has been reported elsewhere.[3] It is the purpose of the present communication to describe normal vascular patterns of the human circle of Willis which can be demonstrated following retrograde injection of the brachial artery, and to discuss certain functional implications that presented themselves during the course of these studies.

METHOD

Brachial cerebral angiography is best performed under local anesthesia.[4] Whereas percutaneous puncture techniques in the cervical region frequently produce unavoidable distress to patient and angiographer, brachial arteriotomy is easily accomplished in comfort. In the past, the problem posed by a frightened, struggling patient during percutaneous puncture of the carotid, vertebral or subclavian artery constituted a positive indication to some physicians for use of general anesthesia as a routine measure. Yet purposeful induction of unconsciousness in a patient with cerebral dysfunction of unknown cause is a hazard better avoided. Patients are much less averse to a small incision in the arm than to insertion of a needle in their neck. It is of interest that when brachial angiography is performed in a patient who had previously undergone percutaneous injection, reaction to the two procedures invariably is favorable to surgical approach in the arm.

A number of advantages is a consequence of the site of arterial cannulation. The patient is able to move about freely during the procedure; positioning of the head and neck with precision is a relatively simple maneuver; and injection of opaque medium produces discomfort mainly in the arm and shoulder where it is better tolerated than in the head. Still other important benefits include avoidance of

* This work was supported in part by a grant from the Tobacco Industry Research Committee.

trauma to major arteries of the cerebrovascular tree; circulation of opaque medium under conditions similar to physiologic flow of blood; and opacification of two-thirds or more of the cerebral circulation subsequent to each injection.

Retrograde brachial injection is carried out in a room especially equipped for such studies. Surgical technique is uncomplicated. The right upper limb is abducted in slight flexion at the elbow; surgical solutions are painted on the shaved upper inner arm; linear infiltration of a local anesthetic is carried out in skin overlying the bicipital groove; a 3 cm. incision is made, subcutaneous tissues are retracted and the neurovascular bundle is identified; then the brachial artery is isolated and lifted on rubber tapes. The artery is incised and a special twelve-gauge cannula* is inserted and anchored in place.

Positioning for the submentovertical view presents no difficulties. Usually these roentgenograms are obtained after completion of the anteroposterior and lateral sequences. The patient lies supine with his shoulders extending slightly beyond the head end of the stretcher-table. The latter is slowly pumped up until the vertex of the hyperextending head barely contacts the surface of the film-changer (Reed's base line parallel to the table). This position is surprisingly comfortable for most patients, and frequently easier to attain in the elderly than even moderate degrees of head flexion. The tube is adjusted so that the 10 cm. protective cylinder is inclined at an acute angle. The mandible of the patient is hyperextended to move it out of the way and the head is immobilized between plastic sponges. Ideally the mandible will then form the boundary along the upper edge of the exposed film sequence.

The time-setting sequence ordinarily is two films during the first second, then three films each second for the next several seconds. Delay roentgenograms are not obtained in the average patient since capillary and venous phases of cerebral circulation in submentovertical projection have not been found to be particularly informative.

* Manufactured by Becton-Dickinson Company, Inc., Rutherford, New Jersey.

DISCUSSION

Roentgenographic studies of the human circle of Willis have awaited a method which would provide successful opacification of anterior and posterior segments of this artery-complex while conditions of flow were maintained as nearly normal as possible. Retrograde cerebral angiography is considered by the author to fulfill for the human, the criteria laid down by McDonald and Potter[5] in their experimental investigation of cerebral circulation in the rabbit —avoidance of occlusion of the arterial lumen and lack of induced pressure changes in the system being investigated. After retrograde injection in the right brachial artery of man, the bolus of hypaque which reaches the subclavian-innominate lumina equilibrates with arterial pressure in a fraction of a second. Blood pressures measured on the opposite arm during and subsequent to injection have not been found to vary significantly. It is most likely, therefore, that following pressure equilibration in thoracic vessels the contrast medium is circulated through the carotid and vertebral systems under hemodynamic conditions normal for the individuals under investigation. Vascular pathways which become visible subsequent to injection in this fashion are believed to be those through which blood circulates in a physiologic setting.

It is not uncommon after retrograde right brachial injection to see in the initial high speed roentgenograms an advance column of diluted opaque medium streaming along the walls of carotid or vertebral arteries. The vessels have not yet been flooded with contrast solution. The central core of each artery remains for an instant translucent, testifying to higher speeds and greater dilutions in this region. During these transient phases, a hint can occasionally be gained of hemodynamics, for with incomplete opacification swirling and spiralling become visible, or laminar flow

at the head of the column can be seen to be interrupted by sudden turbulence. These features vanish with arrival of the main body of opaque medium, although they sometimes reappear intracranially when concentrated contrast solution in the vertebral artery meets a diluting stream at the basilar artery.

When the 50 per cent hypaque solution is undiluted by blood, limits of vessel size for visibility are surprisingly small. It is not infrequent that terminal branches of small arterioles (200–300 μ) are sharply opacified. Peculiarities of vessel structure, branching, and progressive filling are easily determined by examining consecutive roentgenograms, and artifacts due to positioning or confusing bone detail can usually be readily distinguished.

Filling and emptying of the human circle of Willis with contrast medium occur quite rapidly in the normal individual. A complete cycle through the anterior segment often takes place in less than two seconds. The speed of film changing is therefore greater for submentovertical projection so as to obtain a clear sequence of fluid flow through the system.

Velocity of blood flow is proportioned to the size of vessel through which it travels. It has been pointed out in a previous paper[3] that serial roentgenograms corroborate this relation between artery luminal diameter and speed of flow. Brachial-cerebral angiograms show a consistent difference in rate of flow through vertebral and internal carotid arteries. Normally, the rapidly moving stream of the internal carotid artery enters the cranium first, and opaque medium has moved well out into peripheral branches of the middle and anterior cerebral arteries by the time the advancing contrast medium-column in the more narrow vertebral artery arrives at the brain stem. This considerable time differential between anterior and posterior segment flow is maintained throughout the cycle of cerebral circulation and it is not uncommon to see opaque substance still within the basilar and posterior cerebral arteries during hemispheral venous phases.

Certain structural and functional components of the human circle of Willis are seen with regularity. There is little variability in the course or relative position of major trunks contributing to the circle, for example. But the origins and distributions of secondary arterial branches are subject to considerable individual difference, making it exceedingly difficult to distinguish normality from abnormality, or developmental difference from effects of vascular disease. Flow patterns of the circle of Willis will be described in patients who have shown no clinical manifestations of cerebrovascular disease. Deviations in structure or function felt to be significant will be commented upon.

Flow Patterns

A typical sequence of filling and emptying within the circle subsequent to retrograde injection of the right brachial artery is shown in Figure 1. Despite manual compression of the contralateral common carotid artery, crossover is not complete in the anterior segment, indicating lack of functional intercommunication between the internal carotid arteries. In the first film, hypaque in the carotid system has streamed several inches beyond the cervical bifurcation, while in the vertebral artery the head of the column has just come into view. One half second later (second film) peripheral branches of the middle and anterior cerebral arteries are well opacified, and contrast substance has reached the basilar artery. Subsequent exposures represent an elapsed time of one and one half seconds, during which fine radicles originating from the superior surface of the basilar artery become visible, and filling occurs in the large left posterior cerebral artery which remains a prominent vessel to the end.

As the basilar drainage opacifies, there can be seen small twigs representing the right posterior cerebral and spinal arteries, and a thread-like channel which is probably the left posterior communicating vessel. *Filling of the left posterior communicating artery represents the sole anastomotic response*

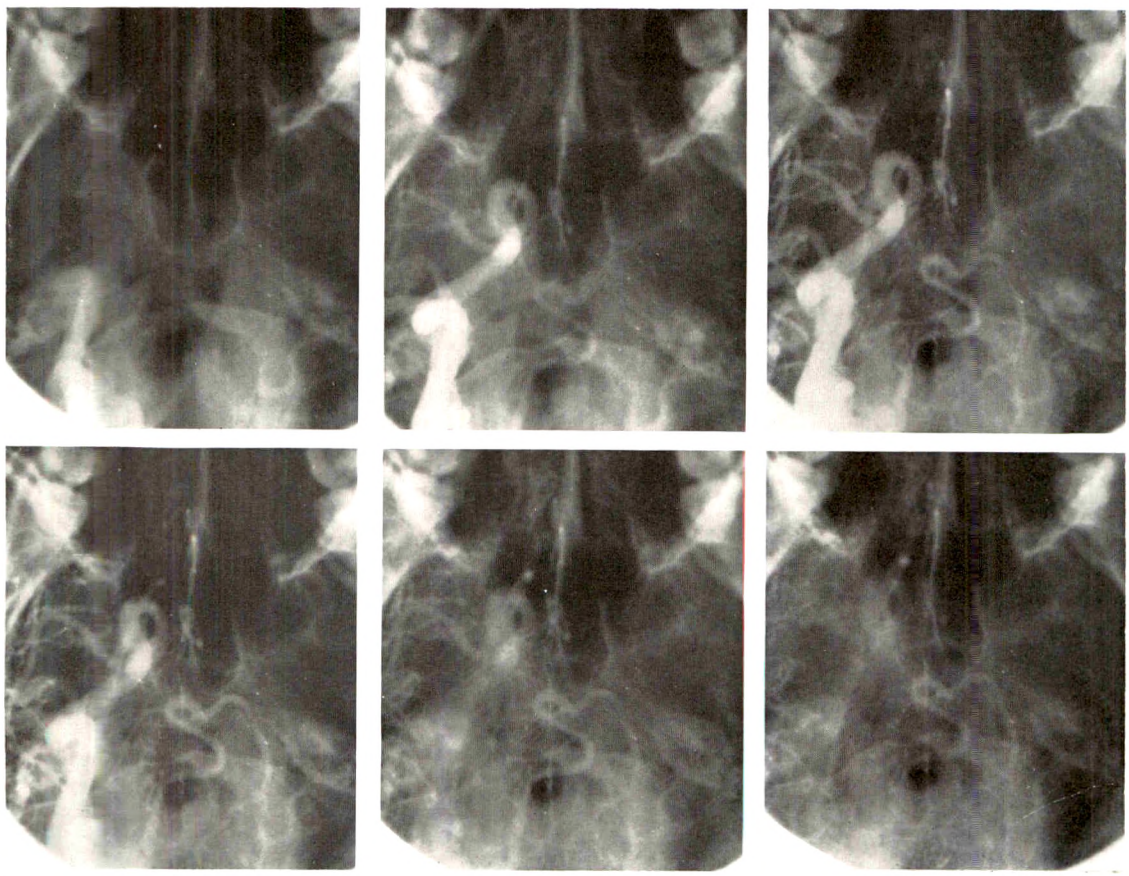


Fig. 1. Retrograde right brachial injection with contralateral carotid compression. Sequence begins at upper left and proceeds left to right. Circulation is normally rapid. Total time required is slightly over two seconds. The anterior segment does not communicate. Note the sharply curved course of the basilar artery and the characteristic persistence of the opaque medium in that circulation. The disproportion in diameter of the two posterior cerebral arteries is somewhat unusual. The anterior cerebral artery is superimposed upon the median nasal septum.

of this circle to marked drop of pressure in the contralateral carotid system. The anterior inferior cerebellar branch is very small. The diameters of vessels can be seen to remain constant throughout the circulatory cycle, and differences in size appear to be a reliable reflection of different hydraulic capacities in various branches of the system. It is noteworthy that the right posterior communicating artery is not visible during any part of the cycle, and also that both anterior cerebral arteries fill from the right side.

The large volume of opaque medium propelled up the carotid artery dissipates rapidly, and comparatively little remains in this system on the final film. Speed of flow in the basilar system is in marked contrast, for opaque substance persists until the end of the film sequence. The total time that contrast medium remains within the anterior segment of the circle is much less than the period for which it lingers in the posterior segment.

In all sequences to date it has been observed that, unless there is arterial obstruction or major structural deviation in the carotid system, posterior segment flow is delayed and relatively sluggish. It has, therefore, been assumed that this is a natural phenomenon. The significance of normally more rapid circulation through drainage fields of the anterior and middle cerebral arteries is as yet unknown.

Examples of different arterial configura-

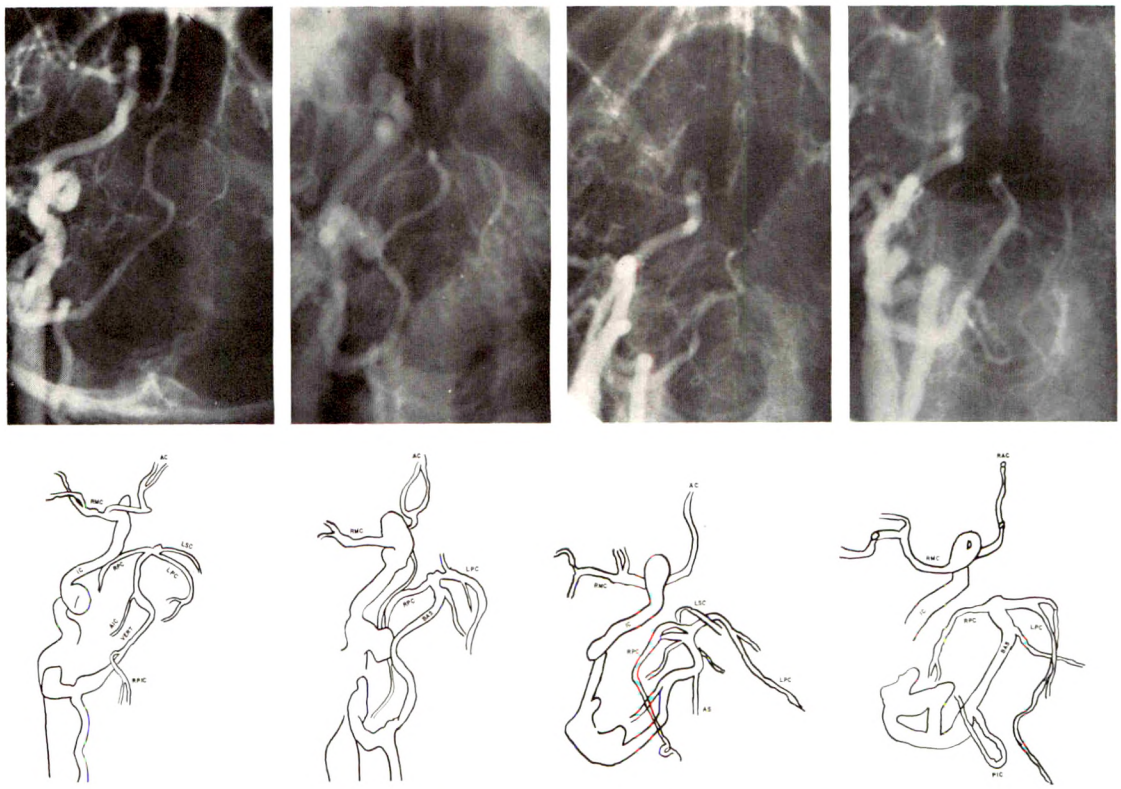


FIG. 2. Configurations of the circle of Willis. Each tracing is of the roentgenogram above. No carotid compression was performed. Note the consistent bilateral filling of the posterior cerebral arteries and the bilateral opacification of the basilar branches. A posterior communicating artery (left) is seen on only one roentgenogram. There is great variability in the site of origin and the course of vessels derived from the basilar artery.

tions of the human circle of Willis during maximal filling are shown in Figures 2 and 3. These patterns are alike in that fluid flow in the anterior segment of the circle remains unilateral despite efforts in some cases to produce anastomotic communication by contralateral carotid compression.

Carotid Trunks. The common carotid artery is seen as a heavy, opaque column extending several inches from the lower margin of exposed film. A fairly abrupt, well-marked narrowing marks the point of cervical carotid bifurcation. The internal carotid artery then ascends vertically a short distance, swings sharply to pass medially in a straight line for about 3 cm., and reverses course to penetrate the floor of the skull. Variations are unusual in the cervical course of these major trunks unless arterial disease is present.

Anterior Cerebral Artery. Opacification of the right anterior cerebral artery is such a constant feature of retrograde angiography that nonfilling is regarded as evidence of occlusive vascular disease or major developmental deviation. The precise incidence is unknown of derivation of both anterior cerebral arteries from one internal carotid, but it must be quite low.[6] In the present series of approximately 50 consecutive cases, including patients with various kinds of cerebral lesions, only two examples were found of dual unilateral derivation (Fig. 1). Multiple channels connecting anterior cerebral arteries are known to be far more common than inadequate communication between these vessels—a situation quite unlike that characteristic of posterior communicating vessels.[1]

During early filling phases the anterior

cerebral arteries overlie and parallel the median nasal septum, whereas a second or so later their terminal branches arch backward and may be superimposed on the circle of Willis itself. Moderately high-speed film shuttling (3/second) allows easy differentiation of these branches from those arising at the circle of Willis.

Posterior Segment Arteries. The vertebral artery displays little variation in its course, and the characteristic cervical loop[4] is well displayed in submentovertical views. A branch of this artery, visible on most angiograms, is the right posterior inferior cerebellar artery (Fig. 2 through 5, inclusive). This vessel arises from the medially ascending limb of the vertebral artery, and follows a highly variable path. On an occasional angiogram a parent trunk of the anterior spinal artery can be seen arising in approximately the same location.

The Basilar Artery. The lumen of the basilar artery normally is completely filled during right brachial angiography. A curving course, sometimes C-shaped and occasionally in the form of an S, is much more characteristic of this vessel than the straight median structure seen in textbook diagrams of the human circle of Willis. Although in some instances of unusual tortuosity, atherosclerosis is undoubtedly a contributing factor, it has been observed that even in young persons free of serious arterial disease the trunk of the basilar artery may be sharply curved to the right or left. The rostral tip of the artery, on the

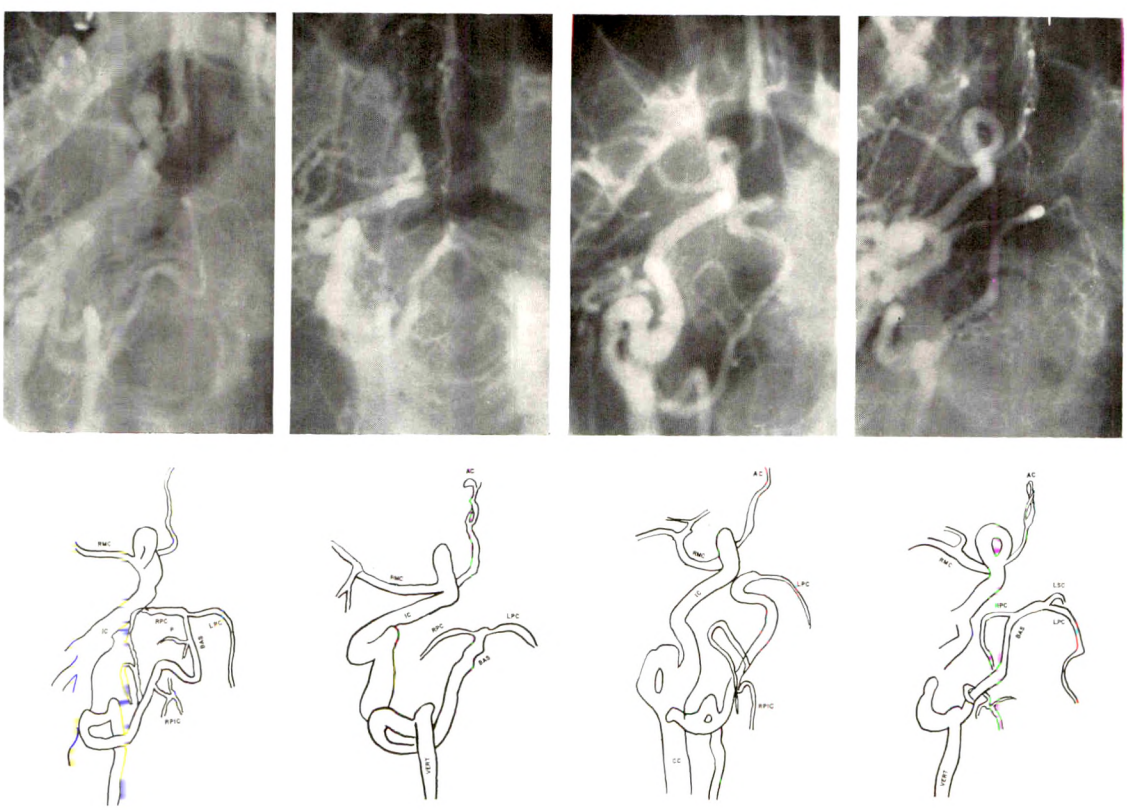


Fig. 3. Configurations of the circle of Willis. Each tracing is of the roentgenogram above. Carotid compression carried out during injection of patient on far right results only in slight reflux into left anterior cerebral artery. Note the wide differences in diameter and variable course of the basilar artery. The right posterior cerebral artery fails to fill in one instance (? pathologic change). The middle and anterior cerebral arteries show little variability in origin or distribution of their main trunks. The posterior communicating arteries are usually not seen.

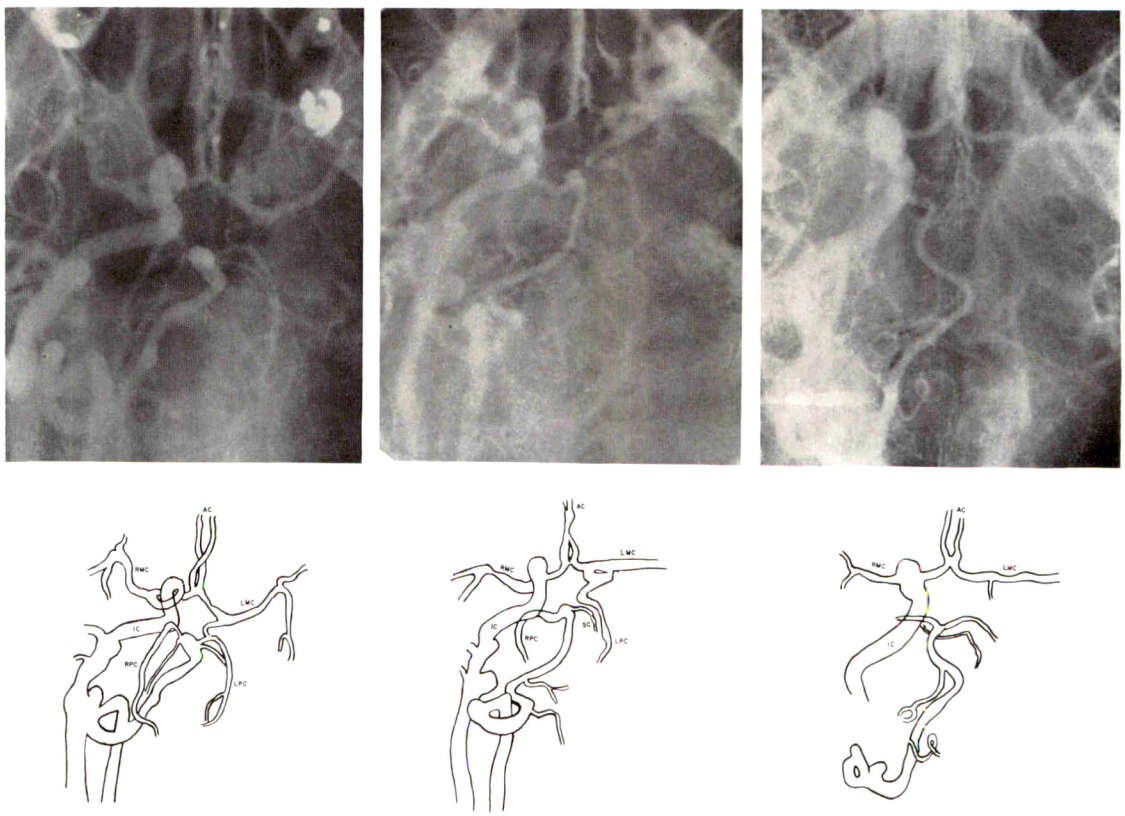


FIG. 4. Brachial retrograde injection with compression of contralateral cervical carotid artery. Filling of the entire anterior segment of the circle of Willis is demonstrated. *Left:* The slender right posterior communicating artery is well seen. Note the symmetry of the two middle cerebral arteries and the apparent transposition of the anterior cerebral arteries. The vertebral artery is of adequate size and the superior cerebellar branches are filled. *Middle:* Note the derivation of the left posterior cerebral artery from the internal carotid artery and the median but narrow basilar artery. *Right:* C-shaped basilar artery with a prominent right posterior cerebral branch.

other hand, varies little in its central anatomic position from patient to patient.

Posterior Cerebral Arteries. Both posterior cerebral arteries can be clearly seen in the usual study. They arise almost always from the rostral end of the basilar artery and appear to be a natural continuation of this vessel. Density of opaque medium is the same in each of the vessels. This bilateral circulation is in marked contrast to that described for animals,[5] and indicates that thorough mixing of the vertebral streams is the rule in the human basilar artery. It is probable that interruption of laminar flow by turbulence at the vertebral-basilar junction is responsible for the phenomenon. The two posterior cerebral arteries demonstrate typically a "weeping-willow" configuration. Major variations are common, and may include bifid origin, early branching, and occasionally what appears to be total absence of one artery (Fig. 2).

Other Basilar Branches. Superior cerebellar arteries are seen with a fair degree of frequency. It is only rarely possible to identify a sequence of lateral branches of the basilar artery similar to those ordinarily diagrammed in texts. This discrepancy cannot be ascribed to physical characteristics of the opaque medium used for angiography, for left-sided basilar branches fill almost as frequently as those on the right, and intracranial arteries of very small

caliber regularly become opacified elsewhere (Fig. 3). As a matter of fact, it is not uncommon during certain arterial filling phases to see fine perforating radicles emerging from the superior surface of the basilar artery, or hair-like pontine branches outlining the external form of the brain stem.

When contralateral carotid compression is carried out, a few seconds before retrograde brachial injection, opaque medium may cross to fill the entire anterior segment of the circle of Willis. This has occurred in perhaps 50 per cent of individuals to date. The distal internal carotids and right and left anterior and middle cerebral arteries are flooded with contrast solution. Shortly thereafter the posterior segment fills via the vertebral artery and all major functional components of the circle can be visualized. Figures 4 to 6, inclusive, show the roentgenographic appearance of the circle of Willis at that instant. Occasionally, similar filling will occur when an excess of opaque medium refluxes proximal to the innominate into the arch of the aorta and passes up the left internal carotid artery (Fig. 6).

Filling of the entire anterior segment of the circle of Willis is excellent evidence of anastomotic response to drop of arterial pressure in the left carotid system, and proof of the existence of adequately patent anterior communicating channels. The more rapid anterior segment circulation results in filling of the entire system bilaterally, before the basilar drainage becomes opacified by arrival of the vertebral stream. There is no evidence that opaque medium



Fig. 5. Right brachial injection and left carotid compression. *Left:* Quadrilateral circle of Willis with unusually thick left posterior communicating artery joining the posterior cerebral trunk. Note the prominent posterior inferior cerebellar branch and the midline basilar artery. *Middle:* Posterior dislocation of the right middle cerebral complex by space-occupying mass. The posterior cerebral and superior cerebellar branches are well outlined. *Right:* Symmetric anterior and middle cerebral arteries with widely-spaced "weeping-willow" posterior cerebral configuration. There are no visible posterior communicating arteries.

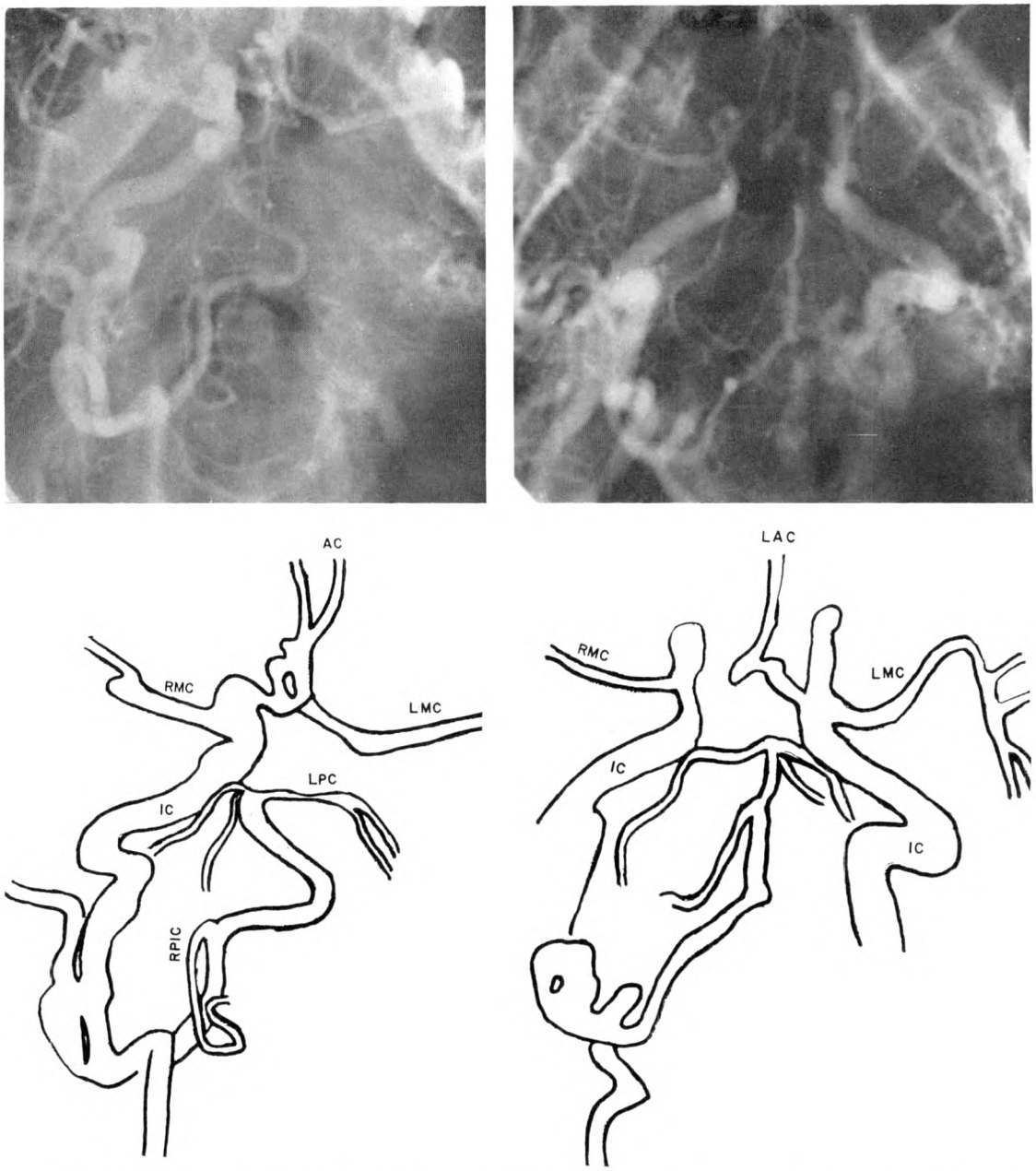


FIG. 6. Brachial injection with left carotid compression. *Left:* Prominent posterior inferior cerebellar artery and almost transversely placed basilar artery are visualized. *Right:* The opaque medium ascends both internal carotid arteries. Filling of the anterior cerebral arteries is seen only from the left. Note the markedly different course of the right and left middle cerebral arteries. There was no clinical evidence suggesting the presence of an intracranial lesion.

flooding the anterior segment under these conditions passes posteriorly to contribute to the basilar circulation nor that circulation in the basilar system compensates for the pressure drop in the left anterior segment. During this type of maximal circulatory stress, therefore, the left posterior communicating artery, at least, fails to respond as an anastomotic conduit. The posterior communicating vessels can rarely

be seen during brachial-cerebral angiography and, in the few instances they are visible, they are of such small caliber that it is difficult to conceive them to be carrying significant volumes of blood.

These observations indicate that the human circle of Willis is functionally a circle in name only. The independent anterior and posterior segments possess major differences in function. Internal carotid flow normally supplies the ipsilateral half of the anterior segment, but about 50 per cent of individuals possess the capacity to maintain adequate functional circulatory flow to both hemispheres by way of one internal carotid artery.

Posterior segment circulation is characterized by bilateral distribution of a relatively small volume of slowly moving arterial blood. The brain stem and cerebellar areas are, therefore, usually isolated from the rapidly moving high volume stream perfusing the anterior segment. In the usual individual if the internal carotid supply fails bilaterally there would appear to be little chance that hemispheral perfusion could be supported by way of posterior segment flow.

SUMMARY

1. Retrograde brachial angiography fulfills experimental criteria established previously in animals for investigation of cerebral circulation. The technique avoids completely pressure artifacts and arterial injury.

2. When the submentovertical projection is combined with brachial injection, clear visualization is obtained of components of the circle of Willis.

3. Typical configurations of human circles are presented, and the influence of contralateral carotid compression is demonstrated.

4. Some preliminary observations are made on functional capacity of the human circle of Willis as demonstrated by this method.

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VALVES OF THE COMMON CAROTID ARTERY DURING ANGIOGRAPHY*

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THE common complications of carotid angiography have been reported in detail and are well known.[1] However, there is one uncommon complication which we feel has not received enough attention—the creation of artificial valves in the common carotid artery during the puncture of this vessel. Sirois, Lapointe, and Côté[6] have published such a case with postmortem findings. The purpose of this paper is to present 4 similar cases and to describe the roentgen findings.

All examinations were performed with a serial cassette changer exposing six films in sequence at one second intervals. The first 3 cases were studied by the percutaneous method while in the fourth case the common carotid was surgically exposed.

REPORT OF CASES

CASE I. J.G. KCH #43553. This twenty-three year old white female entered the hospital on September 19, 1958 because of vaginal bleeding. The patient had had her last menstrual period three months before. According to the history she had suffered a generalized convulsion of five to ten minutes' duration a few hours before admission. There were no sequelae. A dilatation and curettage were performed on the following day. Six hours after operation the patient had a generalized convulsion following which she was unresponsive for a period of three days. Lumbar puncture performed during this period revealed xanthochromic spinal fluid. She subsequently became alert and there were no neurologic signs except nuchal rigidity.

Left carotid angiography was performed on September 30, 1958. No contrast material was seen intracranially until the five second angiogram. It was therefore suspected that there was a partial block in the cervical portion of the internal carotid artery. The films were then positioned for study of the neck and the examination was repeated. On this study the early angiograms revealed the contrast material to stop abruptly in the distal portion of the common carotid artery (Fig. 1). The head of the contrast column had a meniscus appearance with concavity directed inferiorly. On the three and four second angiograms the vertebral artery was faintly opacified. At five seconds (Fig. 2) the contrast material started to escape the block and eventually opacified the internal, external, and branches of the middle cerebral arteries. However, most of the contrast material remained in the distal portion of the common carotid artery and maintained the meniscus appearance on its upper border. A repeat examination performed immediately revealed the same findings. By October 5, 1958 the patient's nuchal rigidity had disappeared and two days later a lumbar puncture revealed clear spinal

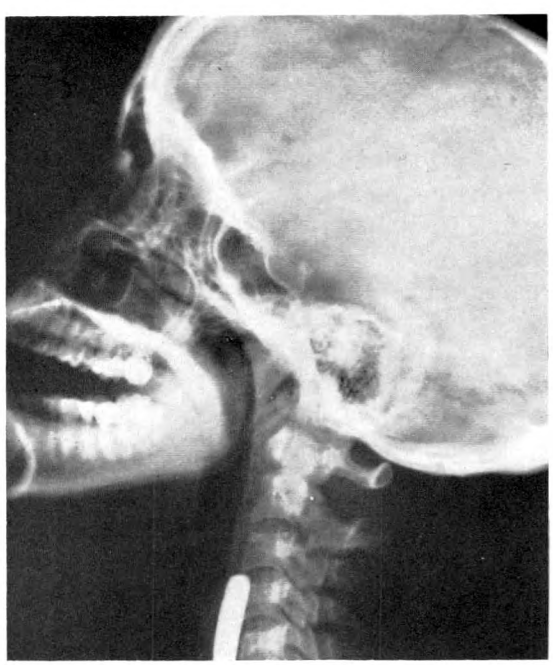


FIG. 1. Case I. Three second angiogram showing contrast material in the common carotid artery.

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fluid with a negative Pandy test. The patient signed her release against advice on October 12, 1958. The discharge diagnosis was subarachnoid hemorrhage of undetermined etiology.

Case II. H.B.N. KCH #49727. This forty-two year old Negro male was admitted because of right hemiplegia and aphasia. While being admitted he developed a grand mal type of convulsion with loss of sphincter tone and went into status epilepticus for about thirty minutes. Toward the end of the convulsive episode the patient was noted to have more prominent convulsive movements on the right side of the body. Following this he was lethargic and pain stimuli caused motion of the extremities on the left side only.

He slowly became fully alert and seventeen days later, on November 6, 1959, left carotid angiography was performed. The operator had difficulty in puncturing the common carotid artery and the first injection was into the soft tissues of the neck. On the second injection it was noted that the needle was low in the common carotid artery and there were several filling defects in the opaque column just above its insertion. The contrast material passed these defects readily but stopped abruptly just below the common carotid bifurcation (Fig. 3). On the five second angiogram the carotid bifurcation was faintly outlined and at six seconds (Fig. 4) it was well outlined. On both these angiograms there was a faint line of radiolucency running across the opaque column just below the common carotid bifurcation. This line of radiolucency corresponded to the area where the opaque column had stopped on the early angiograms. In the anteroposterior projection it was noted that the common carotid artery appeared to be ballooned just below its bifurcation. Retinal artery pressures recorded on November 9, 1959 were 147/67 gm. in the right eye and 144/60 gm. in the left eye.

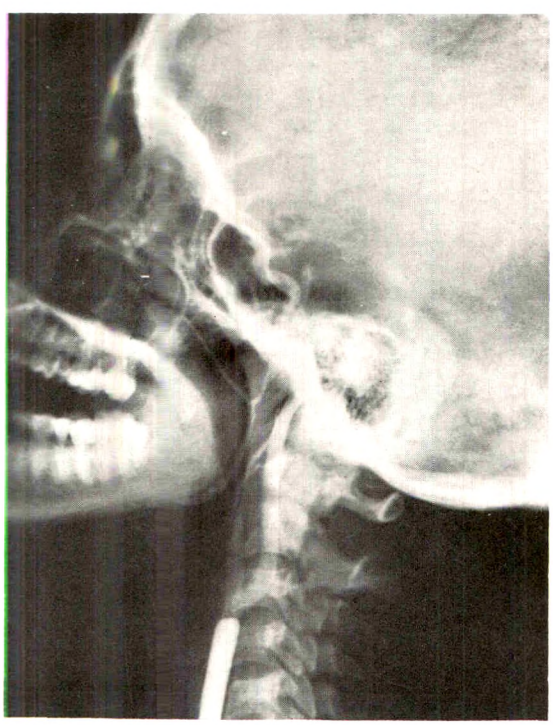


Fig. 2. Case I. Five second angiogram showing some contrast material escaping the block in the common carotid artery.

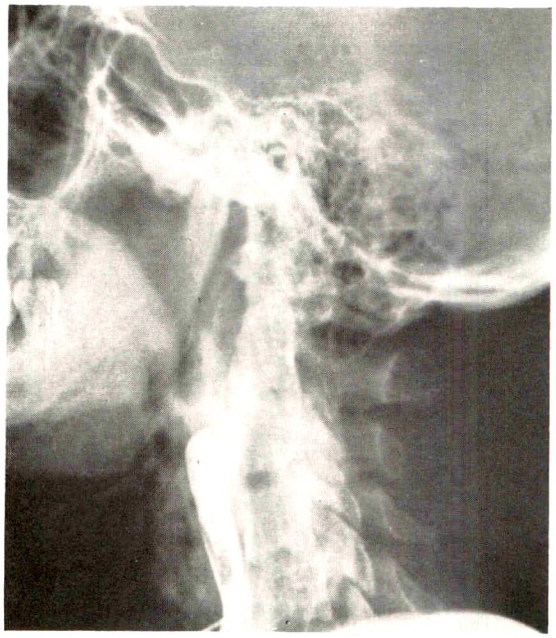


Fig. 3. Case II. Three second angiogram showing numerous filling defects in the common carotid artery. The opaque column has a rounded upper border.

The left carotid angiography was repeated four days later. At this time there was a smooth, rounded, elongated filling defect on the posterior aspect of the opaque column in the common carotid artery. This was apparently caused by a hematoma from the previous examination. Whether it was retrocarotid or intramural could not be determined. Above the defect a curved line of radiolucency arose from the posterior surface of the common carotid artery at the bifurcation and extended anteriorly and inferi-

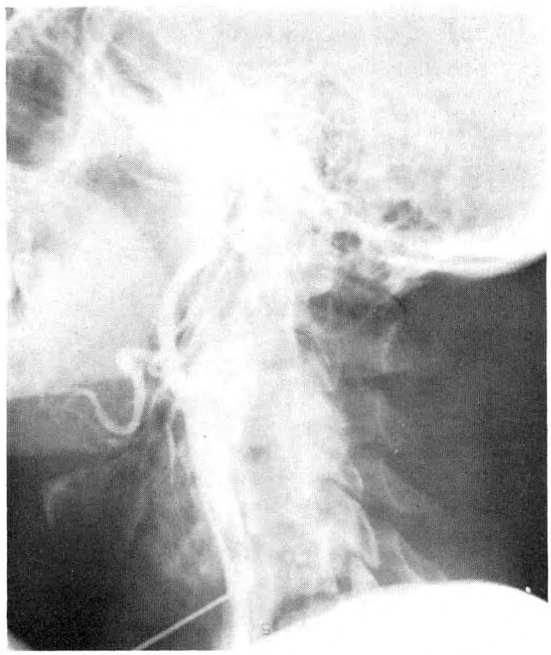


Fig. 4. Case II. Six second angiogram showing opacification of the carotid bifurcation. There is a faint line of radiolucency just below the bifurcation.

orly to become lost in the defect. There was no obstruction to the flow of the contrast material and a normal cerebral angiogram was demonstrated. The retinal artery pressures measured on November 16, 1959 were equal. A pneumoencephalogram on November 18, 1959 was normal.

Left carotid angiography was again performed on December 14, 1959 (Fig. 5). At this time the previously described filling defect had become slightly flattened but was still quite apparent. It was now felt that this was an intramural hematoma which was undergoing organization. The curved line of radiolucency could still be seen, although it was not as prominent as on the previous study. The patient was eventually discharged with the diagnosis of a convulsive disorder of unknown etiology.

Case III. C.C. KCH #5056. This fifty-one year old Negro male was a chronic alcoholic and had been drinking heavily on the night prior to admission. He was found lying in bed on the day of admission in a stuporous condition. Information from a friend disclosed that the patient had been suffering from "circulation" in the legs recently. Upon admission he was stuporous and in shock. There was spasticity of both lower extremities, somewhat more marked on the left. There was a positive left Babinski toe sign. During the next two days the spasticity of the lower extremities decreased markedly and the Babinski toe sign disappeared. The patient remained stuporous. Lumbar puncture on the third hospital day (February 3, 1960) revealed clear fluid with a negative Pandy test and no cells.

Right carotid angiography was performed on February 4, 1960. Angiograms taken in the anteroposterior projection revealed the contrast material to stop abruptly in the distal portion of the common carotid artery (Fig. 6). The head of the opaque column had the appearance of a meniscus with its concavity directed inferiorly. In addition there was a faint crescentic line of radiolucency about 1 cm. below the point of the needle. In the early angiograms the contrast material flowed in a retrograde direction to opacify the right subclavian, innominate, and right vertebral arteries. In the four second and five second angiograms (Fig. 7) the contrast material slowly escaped the block and outlined an area of irregularity in the proximal portion of the internal carotid artery. A second needle was then inserted higher up in the common

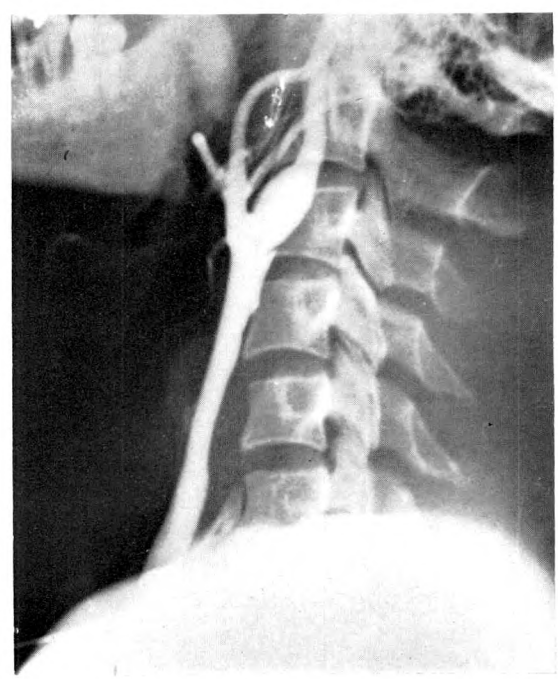


Fig. 5. Case II. Angiogram made five weeks after Figures 3 and 4. The valve can be faintly seen. The smooth filling defect on the posterior aspect of the artery is apparent.

carotid artery and a repeat study was performed (Fig. 8). This showed an apparently normal carotid bifurcation and normal internal and external carotid arteries. Left carotid angiography was then performed and was negative. Both anterior cerebral arteries filled and were midline. There was no opacification of the right internal carotid bifurcation or right middle cerebral artery.

The patient was taken to the operating suite a few hours later and under local anesthesia the right common carotid, the bifurcation, and internal and external carotid arteries were exposed. Inspection showed that there were adequate pulsations in these vessels. A linear incision was made in the anterior aspect of the common carotid artery, the bifurcation, and the proximal segment of the internal carotid artery. There was a fresh intramural blood clot dissecting between the intima and media of the posterior wall measuring about 1½ cm. long, 4 mm. wide and 3 mm. thick. The clot was removed without difficulty. The artery was closed in two layers, intima to intima and media to media. Following the removal of clamps there were good pulsations in all the exposed arteries. Postoperatively the patient remained stuporous for twenty-one days. When he finally regained consciousness his sensorium remained clouded and he had a spastic quadriplegia.

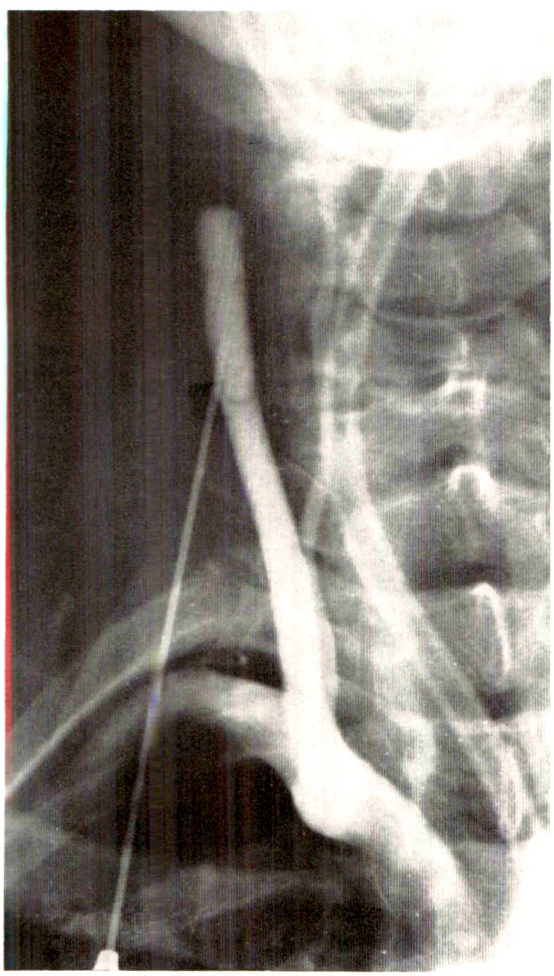


Fig. 6. Case III. Early angiogram showing abrupt stoppage of the contrast column below the carotid bifurcation and retrograde flow through the subclavian, innominate and vertebral arteries. Note the curvilinear line of radiolucency just below the point of insertion of the needle.

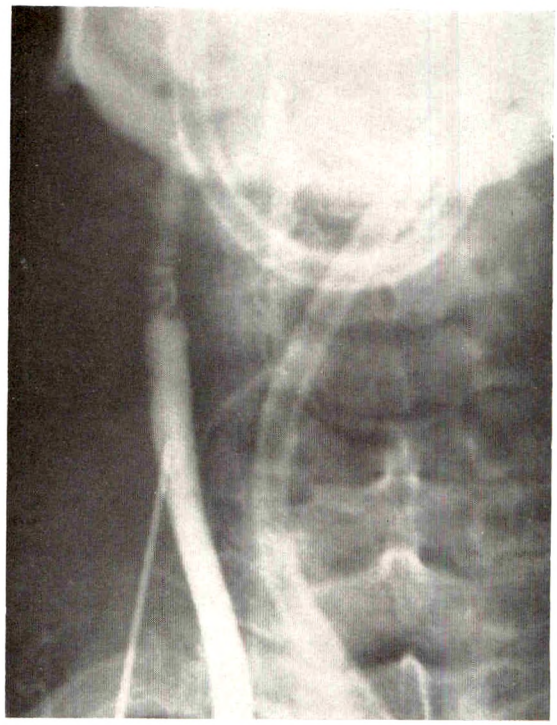


Fig. 7. Case III. Angiogram shortly after Figure 6 showing contrast material outlining a filling defect above the point of previous blockage.

The right carotid angiography was repeated on April 27, 1960 (Fig. 9). This study showed a small area of irregularity in the proximal portion of the internal carotid artery which presumably represented postoperative changes. In addition, on the lateral view there was a line of radiolucency lying just anterior to the posterior border of the distal portion of the common carotid artery. The patient's condition did not improve and he was eventually transferred to a State hospital.

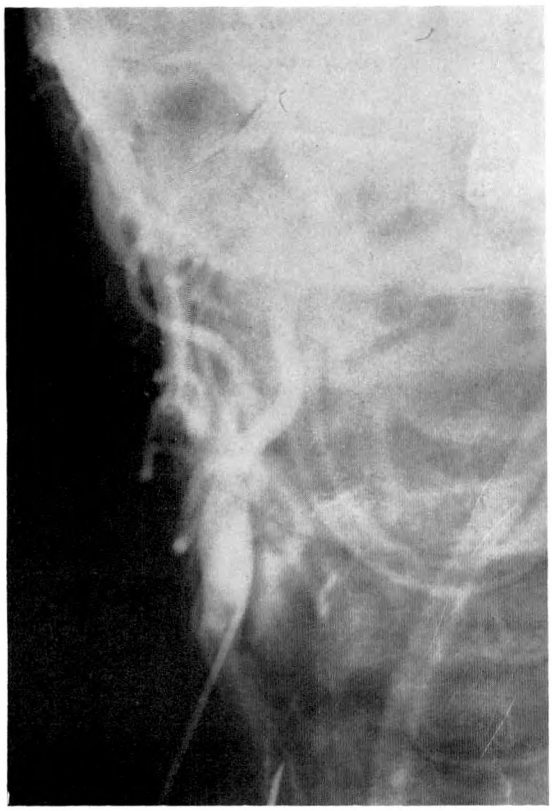


Fig. 8. Case III. A second injection has been made above the block seen in Figure 6 and a normal bifurcation is demonstrated.

Case IV. F.T. This fifty-two year old white male had been suffering from mild attacks of coronary insufficiency for the past ten years. He had had five hospital admissions during the period from October, 1956 to November, 1959, always with the chief complaint of sudden onset of unconsciousness not connected with any convulsive movements, and always with a negative neurologic examination. Because of the possibility of a cerebral vascular insufficiency syndrome, bilateral carotid angiography was performed in November, 1959 using the open technique.

Examination of the early right carotid angiograms revealed the contrast material to stop abruptly in the common carotid artery. The upper border of the opaque column had the appearance of a meniscus with the concavity directed inferiorly. On the three second and four second angiograms the vertebral artery was opacified. On the five (Fig. 10) and six second angiograms a small amount of the contrast material was seen to have escaped the block. However, most of the contrast material remained proximal to it.

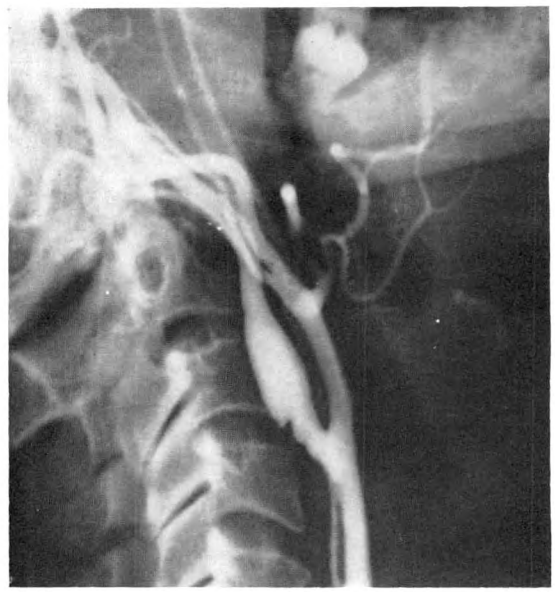


Fig. 9. Case III. Angiogram made eleven weeks after Figures 6, 7, and 8. A valve can be seen in the upper portion of the common carotid artery and an operative defect in the proximal portion of the internal carotid artery.

The patient was later taken to the operating suite and the right common carotid artery and

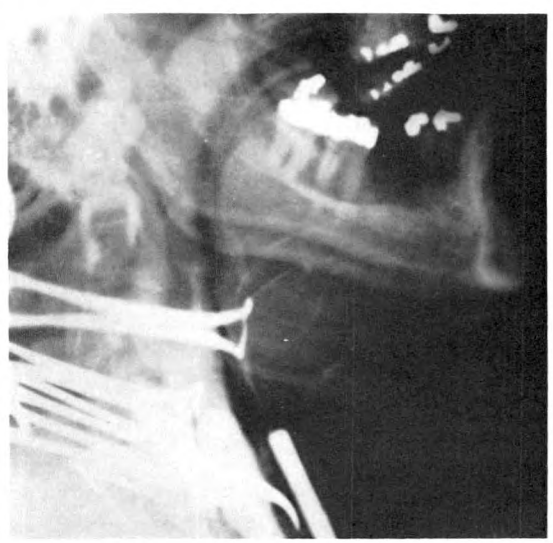


Fig. 10. Case IV. Five second angiogram showing that most of the contrast material is in the common carotid artery and that the column has a rounded upper border. Some opaque medium is escaping the block to faintly outline the carotid bifurcation.

its branches were exposed. There were numerous adhesions behind the common carotid which were considered to be pathologic. There was an oval circumscribed bluish area approximately 2×1 cm. in the medial wall of the vessel about 3 cm. below the bifurcation. This was believed to represent a local infarct of rather recent origin. In addition there was a ridge of scar tissue on the anterior aspect of the common carotid about 2 cm. below the area of infarction. There was no evidence of atheromatous change at palpation and powerful pulsations were felt in the common carotid, internal carotid and external carotid arteries. It was also noted that the distal portion of the common carotid artery just below the bifurcation was approximately twice the diameter of the more proximal portion of this artery. No attempt was made to open the carotid vessels.

DISCUSSION

We agree with Sirois *et al.*[6] that the angiographic appearance in these cases is caused by the formation of a valve. The point of the needle first pierces the intima on the posterior wall of the common carotid artery (Fig. 11). This is followed by a lateral movement of the needle slicing the intima in a crosswise direction. The pressure of the blood flow then elevates the intima and strips it from the media to form a valve. The tip of the needle thus comes to lie inferior and posterior to the lip of the valve. At this point the valve does not entirely occlude the lumen of the artery (Fig. 12). When the contrast material is forcefully injected, the valve is elevated further, coming into contact with the anterior wall of the artery and completely occluding the vessel. During this period the artery may appear to be ballooned just below the block and contrast material may opacify the vertebral artery by retrograde flow. The outline of the head of the contrast material in the common carotid artery is that of a meniscus with the concavity directed inferiorly. This condition lasts for three or four seconds and then the contrast material starts to escape around the valve as the pressure of the injection diminishes and the pressure in the common carotid artery returns to normal. We then see faint

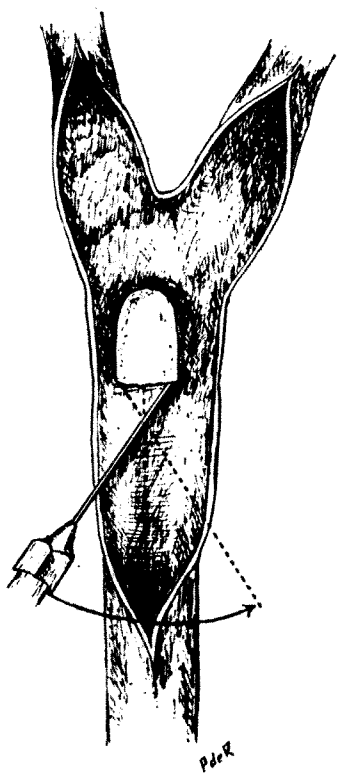


FIG. 11. Diagram showing how the intima of the posterior wall of the common carotid artery is sliced in a crosswise direction. (Reproduced with permission of the authors and *Journal of Neurosurgery*.[6])

opacification of the bifurcation and proximal portions of the internal and external carotid arteries. However, most of the contrast material remains trapped proximal to the valve.

The faint crescentic line of radiolucency seen below the point of the needle in our

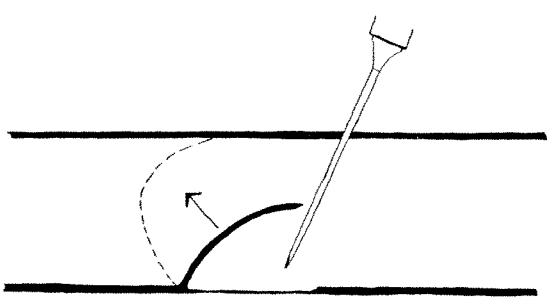


FIG. 12. Line drawing showing the valve in profile. The dotted line represents the position of the valve during and immediately after injection.

third case has also been described by Sirois and co-workers.[6] It is apparently the edge of the elevated intima. This finding cannot always be distinguished on the angiograms. The ballooning of the distal portion of the common carotid artery is likewise not always present. This latter sign may depend on the direction in which the opening of the needle is facing. If it is directed superiorly the contrast material will be forceably injected into the blind sac formed by the valve, thus causing expansion of the arterial wall. If it is facing inferiorly the force of the injection will be dissipated to a great extent against the blood flow and the arterial wall may not dilate.

The most reliable signs of the presence of a valve are the meniscus appearance of the upper border of the contrast column and the eventual escape of a small amount of the material, revealing a normal bifurcation, while the major portion remains proximal to the area of obstruction.

Review of 1,224 angiograms in our series has revealed only 3 cases of valve formation, giving an incidence of slightly less than 0.25 per cent. Because adverse signs and symptoms are rare following carotid artery puncture, we are probably unaware of the actual incidence of intimal damage without valve formation as a result of the procedure. This may be much higher than is suspected. Rowbotham *et al.*[5] performed postmortem examinations on 6 patients within ten days after they had undergone carotid angiography. In all cases the intima on the posterior wall of the carotid vessels had received one or more lacerations up to 3 mm. in length. In one instance there was a hemorrhage in the media 1 cm. long and 5 mm. across. This would correspond to our Case II and Case III. In another of their cases, there was a friable thrombus projecting into the lumen of the vessel from one of these lacerations.

If a valve of the common carotid artery is suspected, a second needle should be inserted above the involved area into the common or internal carotid artery. This was done in our third case but we failed to realize the significance of a normal carotid bifurcation. The measurement of retinal artery pressures may also suggest the presence of this condition. If there is not more than a 15 per cent difference in the systolic retinal artery pressures, occlusion of the common carotid artery is unlikely.[4] Our Case II should have indicated this to us. Pressure on the contralateral carotid artery, as advocated by Gurdjian and coworkers,[2,3] may also be of help in the detection of this condition.

SUMMARY

1. Four cases of artificial valves of the common carotid artery are presented.

2. An artificial valve is formed during carotid angiography by the needle piercing the intima of the posterior wall of the common carotid artery and moving in a crosswise direction. The intima is then elevated and stripped from the media by the pressure of the blood flow, thus forming a valve. This valve causes a partial obstruction to blood flow under normal conditions and a complete obstruction under the abnormal conditions produced when the contrast material is injected.

3. If a valve is suspected, a second needle may be inserted higher up in the common carotid artery or in the internal carotid artery. Measurement of the retinal artery pressures and compression of the contralateral common carotid artery may also help to rule out an occlusion.

4. This lesion is important not only because it may lead to the erroneous diagnosis of an occlusion of the common carotid artery but also because of its possible sequelae, namely, dissecting hematoma and thrombus formation.

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THE ROENTGEN IMAGE OF THE SUBCLAVIAN ARTERY IN THE PULMONARY APEX

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THE subclavian artery may cast a shadow in either pulmonary apex and can be recognized as such on a roentgenogram of the chest. In a review of 300 normal chest roentgenograms it was seen in one apex or in both apices in 40 per cent of the cases. It was more commonly observed on the left than on the right side, the approximate incidence being 2:1. It appears as a curved homogeneous shadow 3–4 cm. in length, sometimes sharply but more often indefinitely delineated (Fig. 1, *A* and *B*). It is projected in one of the four proximal posterior intercostal spaces, most commonly in the second and third; however, it may be completely or partly obscured by the ribs. When it is distinctly outlined, it can be followed on the left as a continuation of the ascending portion of the subclavian artery. This portion is commonly seen, together with the common carotid artery, as a homogeneous shadow just to the left of the air column in the trachea. On the right, the subclavian artery may be identified as a branch of the innominate artery.

REVIEW OF THE LITERATURE

In a contrast study on a cadaver, Assmann[2] has demonstrated that the shadow described above is that of the subclavian artery. Since the advent of angiographic contrast studies *in vivo*, the location and the appearance of the opacified subclavian artery on chest roentgenograms has become well known. A well-documented paper on this subject was presented by Poker and associates.[8] Nevertheless, the identification of the subclavian artery with the shadow seen on plain chest roentgenograms was not made. Poker and associates state that "Roentgenographically, the subclavian arteries are invisible in frontal and lateral views. However, the left subclavian artery can be visualized in the left anterior oblique view. . . ."[8] The last sentence of the quoted statement refers to the first portion of the artery, which represents the

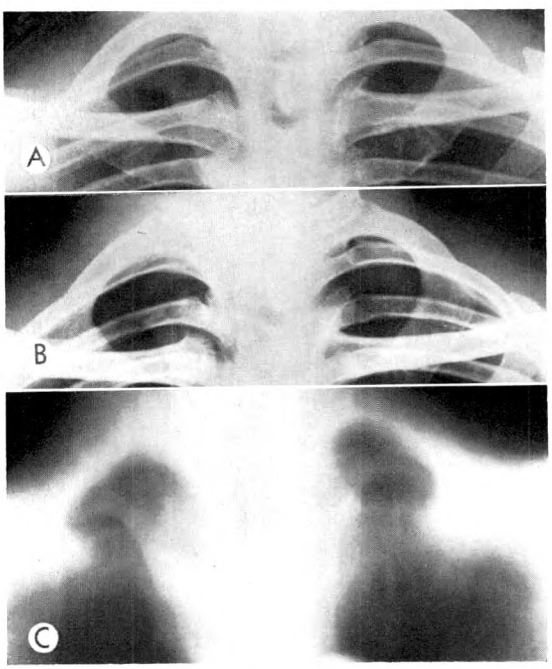


FIG. 1. (*A*) In the right apex, the innominate artery and its bifurcation into the subclavian and common carotid artery are visualized. In the left apex, the first part of the subclavian artery shows calcification in its wall. Because of the angle of projection, the second part is obscured by the second rib. (*B*) In the same patient as *A*, but using a different angle of projection with the tube centered lower, the innominate artery can be recognized in the third intercostal space. Its bifurcation is obscured by the third rib. The right subclavian artery produces a "haziness" in the second intercostal space. The left subclavian artery is well visualized in the second intercostal space. Compare with the left subclavian artery in *A*. (*C*) A laminagram in which both subclavian arteries are visualized also shows origin of the left internal thoracic (mammary) artery as a prominence on the lateral aspect.

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anterior border of the triangular clear space formed with the spine and the aortic arch and seen in this view.

Some of the standard textbooks and monographs[2,6,12,13] of diagnostic roentgenology describe and identify the shadow of the subclavian artery in accordance with Assmann's suggestion, others[7,9–11] seem to ignore it. Caffey's[3] authoritative textbook on pediatric roentgenology describes and illustrates a shadow as "the companion shadow of the left second rib" in the left apex which, by Assmann's criteria and by the observations of the present study, is considered to represent the subclavian artery. Caffey considers this "companion shadow" to be the product of the heavy subcostal muscles on the internal aspect of the left second rib. The "companion shadow," first described by Albers-Schönberg[1] (1908), has been a controversial subject in the literature. According to one concept[4] it represents the proximal border of the pulmonary apex; another explanation[5] is that the shadow is produced by extrapleural structures (subcostal muscles, the last cervical sympathetic ganglion, the supreme thoracic artery and vein and the first thoracic nerve). Apparently the shadow produced by the subclavian artery, as suggested in the present paper, was also interpreted as the "companion shadow of the second rib."

The present paper has two purposes: (1) to re-emphasize the accuracy of Assmann's original observation that the second portion of the subclavian artery may be visualized in the projection of the pulmonary apex in the posteroanterior view of the chest; and (2) to record additional observations.

GROSS AND ROENTGEN ANATOMY

The left subclavian artery is a branch of the aorta and the right is a branch of the innominate artery. The first part of the left subclavian artery runs posteriorly and somewhat laterally to the thoracic portion of the common carotid artery. This segment together with the common carotid artery is commonly seen in the chest roentgenogram just lateral to the translucent air column in the trachea. Then the left subclavian artery turns toward the left. The right subclavian artery reaches a somewhat higher level than its counterpart; nevertheless, this vessel is considerably shorter than the left because of its different origin. The proximally most prominent part of the subclavian artery is located behind the scalenus anterior muscle. From here the artery continues as far as the lateral border of the first rib to become the axillary artery. Thus the scalenus anterior muscle divides the subclavian artery into three parts, the second being the one covered by this muscle. This portion measures approximately 2 cm. in length and is mainly responsible for the shadow in the pulmonary apex. The rest of this shadow is made up of the adjacent portions of the first and third parts of the artery.

Visualization on the roentgenogram is caused by a groove of variable depth in the apex of the lung. This groove decreases the sagittal diameter of this area of the lung compared to that of the adjacent portions of lung and determines the density of the contrasting shadows on the roentgenogram. The difference in the depth of the groove in different persons is one of the reasons why the shadow may be demonstrated in one person and not in another. The less frequent incidence of a visible vascular shadow on the right is the result of the asymmetry of the anatomy of the lungs. The groove on the right side is generally more shallow than that on the left; the relatively higher position of the second part of the artery on this side probably represents a contributing factor. Occasionally, on roentgenograms of excellent quality, particularly on laminagrams, the origin of the internal thoracic artery (internal mammary artery) can be seen on the inferior aspect (Fig. 1*C*). This branch of the subclavian artery arises from the inferior surface of the first part opposite the thyrocervical trunk.

The caliber of the subclavian artery has

been determined by angiocardiographic studies; the average is given as 0.9 cm.[8] Measurements performed in a small number of our cases on conventional chest roentgenograms showed a range of 0.9–1.1 cm., the average being approximately 1.0 cm. This somewhat higher average is explained by the fact that these measurements include not only the lumen but the wall of the vessel as well.

A clear definition of the subclavian artery can be obtained only when both the superior and inferior contours are visualized. In cases where the two contours are obscured by the ribs or are poorly defined because of the angle of projection, the shadow presents itself as a "diffuse haziness" (Fig. 1*B*). The demonstration of the subclavian artery is greatly influenced by the anatomy of the thorax, the width of the intercostal spaces, and the projection angle employed. It was found that a slight cephalad angulation of the central beam (with the tube placed in a lower position) results in better visualization of the subclavian artery in the posteroanterior view than by the usual method (Fig. 5, *A* and *B*). A similar result can be obtained in the anteroposterior view by using a caudally tilted tube, a technique originally employed by Albers-Schönberg for visualization of the pulmonary apex. The same projection is used for anteroposterior roentgenograms of the cervical spine, and the subclavian artery is commonly depicted on these roentgenograms if the pulmonary apex is included.

CORRELATIVE ROENTGEN FINDINGS

Although Assmann's autopsy study and modern angiocardiographic observations locate the subclavian artery where the questionable shadow can be seen on plain roentgenograms, the identification cannot be made with absolute certainty. In the present study we collected material other than angiocardiographic studies with the purpose of adding further support to this concept and possibly eliminating any doubt that the apical shadow in question represents the subclavian artery.

1. Calcium salt deposition in one part of the wall (the media) of the subclavian artery may produce a contrast effect similar to that of an angiocardiographic study (Fig. 2). In the case where the calcium salt deposition is not evenly distributed, the direct continuity of the calcific shadow with the soft tissue shadow of another part of the artery identifies the latter as the subclavian artery (Fig. 3, *A* and *B*). By the dotted line and the plaques produced by the calcification, nature provides an illustration comparable to an anatomic drawing. This "illustration" provides more convincing evidence than any contrast study could produce.

2. In pneumothorax the subclavian artery is visualized against the background of the air-containing pleural cavity (Fig. 4). Because of the increased contrast, the artery is seen more clearly than in a normal chest, although the physical factors are the same since the sagittal diameter of the pneumothorax cavity at the level of the subclavian artery is shorter than that of the adjacent area because of the persistence of the groove on the parietal pleura after the collapse of the lung. In emphysema, pneumatocele and cystic disease a similar situation may exist, the contrast being effected

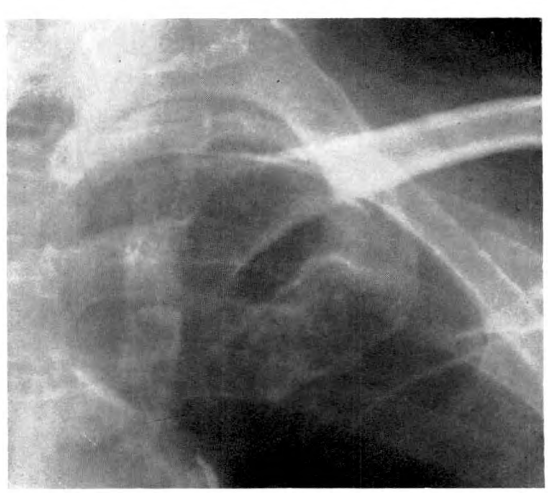


FIG. 2. Extensive calcification in the wall of the left subclavian artery. Note that both the first and the second parts of the artery can be identified.

by the proportion of lung tissue to the air content of the lung in the area of the apex (Fig. 5, *A* and *B*). In any infiltrative process of the pulmonary apex the contrast decreases and the subclavian artery shadow becomes obscured.

3. Laminagraphy is an excellent method for demonstration of the subclavian artery (Fig. 1*C*). The shadow in question is best visualized in cuts where the groove of the subclavian artery is located in the anterior aspect of the pulmonary apex. This cut is usually at a distance of $9\frac{1}{2}$–11 cm. from the posterior wall. Demonstration of the artery is more frequent by this technique than by conventional roentgenography.

CLINICAL SIGNIFICANCE

The shadow of the subclavian artery may be incorrectly interpreted as pulmonary infiltration or thickening of the apical pleura. If calcification is present in the wall of the vessel, this may erroneously be considered to be due to tuberculosis or histoplasmosis. In doubtful cases an effort should be made to clearly define the vascular shadow in an attempt to confirm or to rule out disease of the lung or the pleura (Fig. 6).

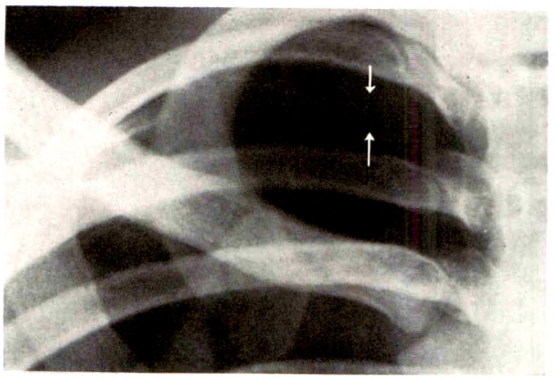


Fig. 4. A right pneumothorax. Note the good delineation of the right subclavian artery.

On the right side, visualization of the subclavian artery may be helpful in identification of the innominate artery. This may be of importance in the differential diagnosis between an elongated or dilated innominate artery and masses of the superior mediastinum. Thus an unnecessary surgical procedure undertaken on the basis of a

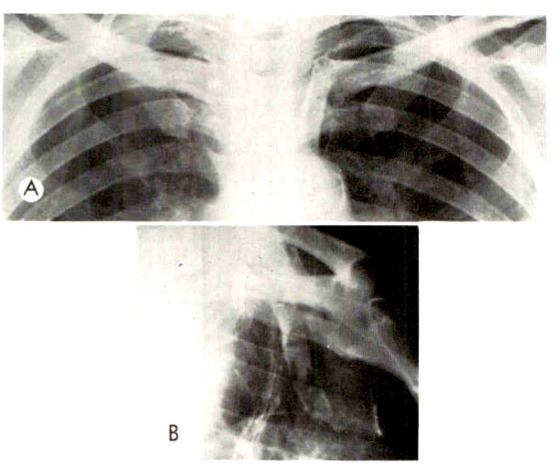


Fig. 3. (*A*) Posteroanterior and (*B*) lateral roentgenograms showing calcification in the wall of the left subclavian artery. In the second part the calcification mainly involves the superior wall, whereas the inferior aspect of the subclavian artery is seen as a "soft tissue shadow." This combination of findings and the lateral view identify the "soft tissue shadow" as that of the subclavian artery. The irregular calcification in the right apex is probably that of the right subclavian artrey.

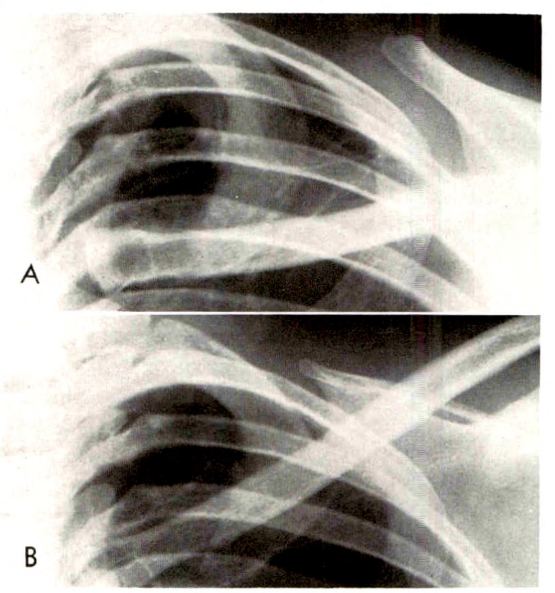


Fig. 5. Cystic disease of the left lung. Note that both the first and second parts of the left subclavian artery are visualized as one continuous structure. (*A*) The artery is clearly visualized in the third intercostal space. (*B*) Using a different projection angle with the tube higher, the artery is partially obscured by the second rib.



FIG. 6. Thickening and a calcification of both apical pleurae. Since the shadows can be followed laterally beyond the medial border of the first rib, this differentiates this finding from shadows of the subclavian arteries.

diagnosis of an "intrathoracic" thyroid can be avoided.

SUMMARY

The subclavian artery (one or both) can be visualized as a curved, band-like soft tissue shadow in the pulmonary apex in about 40 per cent of plain chest roentgenograms. This was first demonstrated by Assmann.[2] Additional observations reported in the present study (laminagrams, plain roentgenograms of cases of calcification in the wall of the artery, pneumothorax, pneumatocele, etc.) provide further support for this concept. Incorrect interpretation of the shadow in question may lead to erroneous diagnosis of apical infiltration or pleural or parenchymal calcification.

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VOL. 86, NO. 6

CINEFLUOROGRAPHY OF CORONARY ARTERY CALCIFICATION*

CORRELATION WITH CLINICAL ARTERIOSCLEROTIC HEART DISEASE AND AUTOPSY FINDINGS

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CINEFLUOROGRAPHY of the heart is the best roentgenologic method for detecting coronary calcification,[8] usually considered direct evidence of coronary artery disease. The purpose of this study was to find any correlation between clinically manifested arteriosclerotic (ischemic) heart disease and coronary calcification as seen at cinefluorography of the heart. Previous roentgenologic studies[7,9,13,16,17,20] without the aid of cinefluorography have been unsuccessful in this respect.

HISTORY

Lenk[9] in 1927 first demonstrated a calcified coronary artery on a chest roentgenogram of a living patient, a sixty-eight year old man with a left ventricular aneurysm and no cardiac symptoms. He hoped that with the Bucky technique and short exposures more coronary calcifications would be seen.

Wosika and Sosman[20] in 1934 reported 2 men and 1 woman with roentgen evidence of calcified coronary arteries, all of whom had angina.

Snellen and Nauta[16] in 1937 collected 40 cases of coronary calcifications; there were 32 men and 8 women, ranging in age between fifty-seven and eighty-five years. Three had calcification of both right and left coronary arteries; 37 had calcification of the left coronary artery only. They used no special techniques or positions, but relied on routine posteroanterior and oblique views of the chest. Seventeen of their patients had cardiac symptoms, mostly angina. The authors felt they could not judge the clinical value of detecting coronary calcification by roentgenography because of the way they had selected their patients.

Sosman[17] in 1943 discussed the technique for locating and identifying pericardial and intracardiac calcifications. He was of the opinion that roentgen evidence of coronary sclerosis did not imply angina but indicated a specific type of damage in a specific place and could be reported only as such. Over a ten year period he found 42 coronary calcifications by fluoroscopy.

Habbe and Wright[7] in 1950 used multiple, high-speed spot roentgenograms to detect coronary calcifications. Over a two and one-half year period they examined every cardiac patient over the age of forty years, taking a minimum of four spot roentgenograms in different positions, and found 28 such cases, 3 per cent of the total cases examined by this method. They added kymography when necessary. They believed that by their method they found twice as many cases as is possible by fluoroscopy alone.

Reich and Witten[13] in 1957 reported 6 patients (5 men and 1 woman) with left coronary artery calcifications. They found the most common site of calcification to be beneath the left heart border in the region of the upper left ventricular contour. Two of their patients had angina and 1 had a coronary occlusion, although 5 of the 6 had negative electrocardiograms.

MATERIALS AND METHODS

Our material consisted of two groups of predominantly white male Veterans Ad-

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ministration Hospital patients, a control group of patients without detectable heart disease and a larger "heart disease group" with suspected or evident cardiac disease including ischemic heart disease.

The control group was made up of 60 men, 15 in each decade from ages forty to eighty, with normal hearts as far as could be determined by histories, physical examinations, electrocardiograms, and chest roentgenograms. These patients were hospitalized for various noncardiac causes. No one with hypertension or diabetes mellitus was included. All underwent cinefluorography for the purpose of detecting coronary calcification.

The heart disease group consisted of 630 consecutive patients, predominantly male, referred to the radiology department for cinefluorography of the heart for suspected or known heart disease of various types. Practically all were cases of acquired heart disease. Cinefluorograms were obtained during the nineteen month period between January 1, 1958 and July 31, 1959, and those showing coronary calcification on the initial reading were reviewed and two factors were studied:

(1) The distribution of calcification between the three main coronary branches, the anterior descending and circumflex branches of the left coronary artery and the right main coronary artery, was ascertained. Due to the difficulty in deciding whether a collection of calcium was in the main stem of the left coronary artery or in the anterior descending branch, all of this calcium was considered to be in the anterior descending branch, since it has been shown that the most common point of calcification is in that branch just distal to the bifurcation of the main left coronary artery.[1,12,15] Calcium in the circumflex branch was usually easy to identify and to locate accurately.

(2) The degree of calcification was determined. This was graded by 2 observers on a one to four plus scale.

The clinical records of all of the heart disease group patients in whom coronary calcification was revealed by cinefluorography were then reviewed for the presence of angina, electrocardiographic evidence of old or new myocardial infarction, and a clinical diagnosis of arteriosclerotic heart disease. The latter diagnosis was reached by the ward physician in practically all cases by considering the usual clinical criteria for that particular type of heart disease and independent of the finding of coronary calcification at cardiac cinefluorography. The same evaluation was made of the records of 80 patients without coronary calcification chosen at random from the heart disease group and the clinical findings of both subgroups were compared. There were 5 women in these two subgroups.

Twenty-one autopsy protocols of patients who had had cardiac cinefluorographies were reviewed. The presence or absence of coronary calcium on each cinefluorogram was correlated with the presence or absence of coronary atherosclerosis and myocardial fibrosis at postmortem examination in the same patient.

The cinefluorographic unit consisted of a Westinghouse five inch image intensifier equipped with a 16 mm. Kodak motion picture camera. The film was Kodak Linagraph Shellburst film in one hundred foot rolls, developed in standard x-ray solutions and dried in air. The cinefluorograms were viewed with a 16 mm. Bell and Howell projector.

Our technique of cardiac cinefluorography,[8] briefly described, consists of six film sequences: (1) in the posteroanterior view, the field sweeps along the right heart border from the diaphragm to the superior vena cava and (2) along the left heart border from the aortic arch down to the left hemidiaphragm; (3) in the right anterior oblique projection, we record from the diaphragm to the pulmonary arteries and then down the left heart border to the diaphragm again; (4) in the left anterior oblique position, the right atrium, the ascending aorta and the mid-cardiac mass are scanned, followed by (5) a record of the posterior border of the heart; finally (6) in the right lateral view a recording of the

posterior border of the heart and the mid-cardiac mass is again obtained.

Usually 30 to 40 feet of film, at the rate of 15 frames per second will record a routine cardiac cinefluorographic examination. At 110 kv., the ma. will fluctuate between 5 and 15 for an average-sized individual. Total radiation exposure averages about 20 r in air, delivered to a constantly changing skin field through a portal 4.75 inches in diameter.

RESULTS

Table I compares by decades the incidence of coronary calcification between the control and heart disease groups. Both groups showed a steady rise in coronary calcification with age up to a peak in the sixty to sixty-nine year group, followed by a drop in the seventy to seventy-nine year group. The slight differences in the percentages between the control and heart disease groups are not significant. Both groups showed an average incidence of coronary calcification of 25 per cent in the forty to seventy-nine year age range. Of the 630 known or suspected heart disease patients on whom cinefluorographies were performed, 150 or 23.8 per cent showed coronary calcification.

Table II shows the age distribution of the 150 patients with coronary calcification and the 80 randomly selected patients without calcification, all within the heart disease group. The sixty to sixty-nine year age bracket contained the largest number of patients in both groups. There were more younger patients among those without coronary calcification than among those with calcium. This produced an average age difference of about ten years (62.4 years as compared to 52.5 years) between the two groups. A comparison of the signs and symptoms of ischemic heart disease between these groups was, therefore, made by decades rather than by total numbers.

Table III compares those patients with coronary calcification and those in whom no calcification was found with respect to incidence of angina, electrocardiographic evidence of old or new myocardial infarction, and clinical diagnosis of ischemic heart disease. Age groups twenty to twenty-nine and eighty to eighty-nine were omitted because of an insufficient number of patients in those decades. The table shows a substantially higher incidence or arteriosclerotic heart disease in all age groups in those

TABLE I

COMPARISON OF INCIDENCE OF CORONARY CALCIFICATION BETWEEN CONTROL AND HEART DISEASE GROUPS BY DECADES

Age Groups	Control Group* 60 Patients (per cent)	Heart Disease Group† 630 Patients (per cent)
20–29		0
30–39		9
40–49	13	8
50–59	27	22
60–69	40	36
70–79	20	32
80–89		40

* No detectable heart disease.

† Suspected or known heart disease of various types including arteriosclerotic.

TABLE II

AGE DISTRIBUTION OF PATIENTS IN HEART DISEASE GROUP USED FOR CLINICAL CORRELATION STUDY

Age Groups	Coronary Calcification: No. in Each Age Group	Coronary Calcification: Per Cent in Each Age Group	No Coronary Calcification: No. in Each Age Group	No Coronary Calcification: Per Cent in Each Age Group
20–29	0	0	5	6
30–39	7	5	12	15
40–49	8	5	15	19
50–59	22	15	13	16
60–69	92	61	28	35
70–79	17	11	6	8
80–89	4	3	1	1
	150*	100	80†	100

* Two females were included in this group.

† Selected at random from those patients in the heart disease group in whom no coronary calcification was demonstrated. Three females were included in this group.

TABLE III

INCIDENCE OF ANGINA, ELECTROCARDIOGRAPHIC EVIDENCE OF MYOCARDIAL INFARCTION AND CLINICAL DIAGNOSIS OF ARTERIOSCLEROTIC HEART DISEASE IN PATIENTS WITH AND WITHOUT CORONARY CALCIFICATION AT CINEFLUOROGRAPHY

Age Groups*	Calcification Seen (150 Patients)			No Calcification Seen (80 Patients)		
	Angina (per cent)	Infarct† (per cent)	Arteriosclerotic Heart Disease (per cent)	Angina (per cent)	Infarct‡ (per cent)	Arteriosclerotic Heart Disease (per cent)
30–39	42.9	28.6	57.1	8.3	8.3	8.3
40–49	50.0	50.0	50.0	13.3§	0.0	0.0
50–59	36.7	18.9	45.5	30.8	15.4	38.5
60–69	41.3	31.5	60.9	21.4	17.8	32.1
70–79	41.2	35.3	52.9	0.0	0.0	16.7

* Age groups 20–29 and 80–89 omitted because of insufficient number of patients in these decades.
† No electrocardiogram available in 4 patients.
‡ No electrocardiogram available in 3 patients.
§ Represents 2 patients with angina due to rheumatic aortic stenosis.

cases where coronary calcium was demonstrated at cinefluorography. This difference was particularly high in the younger age brackets, thirty to thirty-nine and forty to forty-nine years.

Table IV shows that the incidence of clinically manifested ischemic heart disease rises in direct relation to the number of coronary branches exhibiting calcium on cinefluorograms. The amount of coronary calcium in any one branch appeared to show no definite correlation with the presence of clinical arteriosclerotic heart disease.

Table V shows the distribution of calcium among the three main coronary branches in 150 patients with coronary calcifications. The left anterior descending branch was the most frequent site of coronary calcification; the right main artery and the left circumflex branch were second and third, respectively. Most of the calcium was usually confined to the proximal por-

TABLE V

DISTRIBUTION OF CALCIUM AMONG CORONARY ARTERIES AS SEEN AT CINEFLUOROGRAPHY IN 150 PATIENTS

Artery	No. of Times Calcified
Left anterior descending artery	136*
Right main coronary artery	59
Left circumflex artery	25
Two arteries	36
Three arteries	13

* Includes calcium in left main coronary artery.

TABLE IV

RELATION OF EXTENT OF CORONARY CALCIFICATION AT CINEFLUOROGRAPHY TO INCIDENCE OF CLINICAL DIAGNOSIS OF ISCHEMIC HEART DISEASE

No. of Coronary Arteries Calcified at Cinefluorography	No. of Patients	No. of Patients with Arteriosclerotic Heart Disease	Per Cent
One	101	53	52
Two	36	23	64
Three	13	11	83
Total	150		

tion of each artery. Two main branches were calcified in 36 patients and all three in 13 patients.

Table VI is a correlation of the presence of calcification at cinefluorography with the degree of coronary atherosclerosis found at autopsy in 15 patients. Table VII shows the correlation between the absence of calcification at cinefluorography and the state of the coronary arteries and the myocardium at necropsy in 6 patients. Table VI shows the exceptionally high correlation of coronary calcium seen *in vivo* with moderate to severe coronary atherosclerosis at postmortem examination. Table VII, on the other hand, indicates that the absence of coronary calcium appears to point to normal coronary arteries. The tables also show that heart enlargement did not appear to interfere with the cinefluorographic recognition of coronary calcium as much as expected.

DISCUSSION

In order to demonstrate even slight amounts of coronary calcification and as many calcifications as possible, a definite sequence of cinefluorography, with all the positions outlined previously, should be used. It is important in ascertaining the presence of coronary calcification to scrutinize the location, movement and form of the calcific deposits.[4,5,8,16]

Examples of location and movement are shown in Figures 1–4. The form of calcium deposition varies from long densities composed of parallel interrupted lines resembling sclerotic extremity arteries to the fleck of calcium seen in a minimally calcified left coronary artery when it is foreshortened in the left anterior oblique view. The curvilinear character of coronary calcifications aids in their detection.

Although with cinefluorography the detection of coronary calcification has been greatly improved as shown by our discovery of coronary calcium in 25 per cent of a group of males without heart disease, the method by no means visualizes all coronary calcium present. Blankenhorn and Stern[3] found that 80 per cent of 76 patients, the majority of whom were over forty years of age and had died of various cardiac and noncardiac causes, showed coronary calcium on roentgenograms of the heart after removal from the cadaver.

The calcium which is demonstrated by cinefluorography seems to consist of larger plaques, probably at least 2 to 3 mm. in size,[3,19] and, judging from our autopsy series as well as other studies,[15,18] its presence indicates considerable intimal atherosclerosis and coronary stenosis at the points of calcification.

There are many factors aside from the small size of the calcification which may be responsible for nondetection of coronary calcification by cinefluorography.[8] These are obesity, cardiomegaly, pulmonary congestion and effusion, pulmonary and pleural disease of noncardiac origin, failure to examine the heart in all positions, and inattentiveness or inexperience on the part of the observer.

The increasing incidence of coronary calcification with age is well known[10,11] and is shown in Table I. The drop in incidence between the seventh and eighth decades in our series, if real, makes one speculate that an increased death rate from ischemic heart disease during the seventh decade may have produced this drop and that perhaps this decade represents a critical period in those with coronary calcification.

We found a much higher prevalence of clinical ischemic heart disease in patients with coronary calcification than in those without calcium (Table III). This difference was even higher than expected. Fifty-eight per cent of 150 patients showing coronary calcium on cinefluorograms were diagnosed as having clinical ischemic heart disease as compared with 39 per cent of a comparable group without coronary calcification.

The direct relationship between the number of calcified coronary branches found at cinefluorography and the incidence of arteriosclerotic heart disease (Table IV) was expected. Not only did 11 of 13 patients

TABLE VI

CORRELATION OF PRESENCE OF CORONARY CALCIFICATION AT CINEFLUOROGRAPHY WITH STATE OF CORONARY ARTERIES AND MYOCARDIUM AT AUTOPSY

No.	At Cinefluorography				At Autopsy		
	Age	Heart Size	Degree of Calcification		Left Coronary Artery	Right Coronary Artery	Myocardium
			Left	Right			
1	66	Generalized enlargement	0	2+	80% occlusion of anterior descending artery; complete occlusion of circumflex	Fresh occlusion 6 cm. from ostium	Scarring
2	64	Left ventricular enlargement	0	2+	Marked atherosclerosis of coronary arteries with numerous areas of pin-point narrowing		Fresh infarct in septum; fibrosis of left ventricular myocardium
3	66	Moderate enlargement	1+	0	Marked atherosclerosis of anterior descending and circumflex arteries	Relatively uninvolved	Complete loss of myocardium along lateral wall of left ventricle
4	68	Generalized enlargement	1+	0	Anterior descending and circumflex arteries densely calcified; maximum narrowing in anterior descending artery 40% of original lumen	Moderate sclerosis; narrowed to 15% of normal	Diffuse fibrosis of myocardium
5	69	No enlargement	1+	2+	Minimal sclerosis at bifurcation; otherwise normal	Ostium 50% narrowed by sclerosis	Normal
6	65	Left ventricular aneurysm	2+	0	Coronary arteries mildly sclerotic but wide open		Normal
7	64	Severe enlargement	1+	0	Moderate to severe atherosclerosis in all branches with scattered calcium in all branches		Thinning over distal two-thirds of lateral wall of left ventricle
8	65	No enlargement	1+	0	80% obliteration of anterior descending artery 2 cm. from ostium; circumflex 50% occluded	80% occluded 2 cm. from ostium	Flabby; microscopic study showed focal scarring and loss of cardiac muscle
9	64	Moderate left ventricular enlargement	1+	0	Lumen of anterior descending artery about 10% of normal; circumflex least affected	Narrowed by 50%	Extensive fibrosis in lower two-thirds of septum and apex
10	60	Left ventricular enlargement	2+	1+	Calcification in anterior descending and circumflex arteries about 4 cm. in length	Calcification in media for 4 cm. beyond ostium	Thinning at apex of left ventricle about 4 cm. in diameter
11	62	Generalized left ventricular enlargement	1+	0	Anterior descending artery severely sclerotic	Normal	Apex of left ventricle thinned to 4 mm.
12	69	Slight enlargement	3+	1+	Coronary arteries showed considerable amount of calcification in their walls but the lumina not appreciably narrowed		Three small patches of hemorrhagic softening in left ventricular wall
13	65	No enlargement	2+	0	Minimal calcification in first 2 cm. of anterior descending branch	Atherosclerosis but no calcium	Negative
14	62	Left ventricular enlargement	1+	1+	Severe calcification of both coronary arteries with marked narrowing but no occlusion		Slight softening of left ventricle posteriorly
15	44	Left ventricular enlargement	1+	0	Coronary arteries widely patent throughout; calcification and stenosis of aortic valve		Normal

Table VII

CORRELATION OF ABSENCE OF CORONARY CALCIFICATION AT CINEFLUOROGRAPHY WITH STATE OF CORONARY ARTERIES AND MYOCARDIUM AT AUTOPSY

No.	At Cinefluorography		At Autopsy		
	Age	Size of Heart	Left Coronary Artery	Right Coronary Artery	Myocardium
1	59	Generalized enlargement	Anterior descending artery markedly sclerotic; lumen of circumflex less than 50% of normal	Extreme atherosclerosis	Large infarct in posterior wall of left ventricle
2	40	No enlargement	Normal	Normal	Normal
3	71	Generalized enlargement	Coronary arteries very patent with no evidence of atheromatous degeneration		Normal
4	51	No enlargement	Normal	Normal	Normal
5	31	Generalized enlargement	Normal	Normal	Thinning of interventricular septum
6	65	Enlarged	Coronary arteries patent except for small segmental narrowing of anterior descending branch about 1.0–0.5 cm. from ostium		Normal

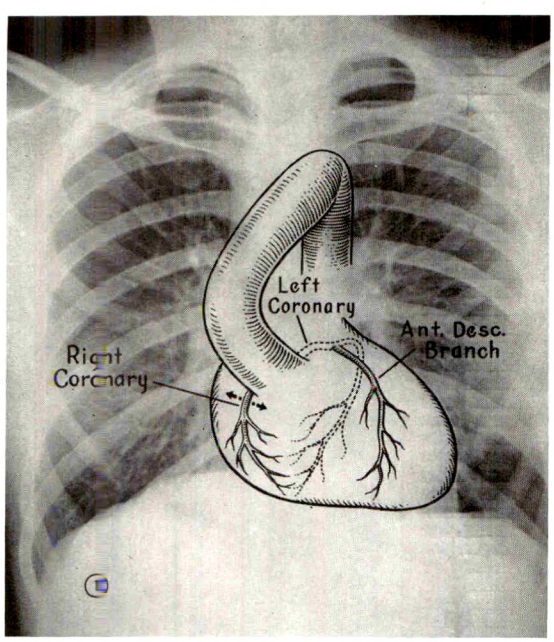


Fig. 1. Posteroanterior view showing the movement and position of the coronary arteries.

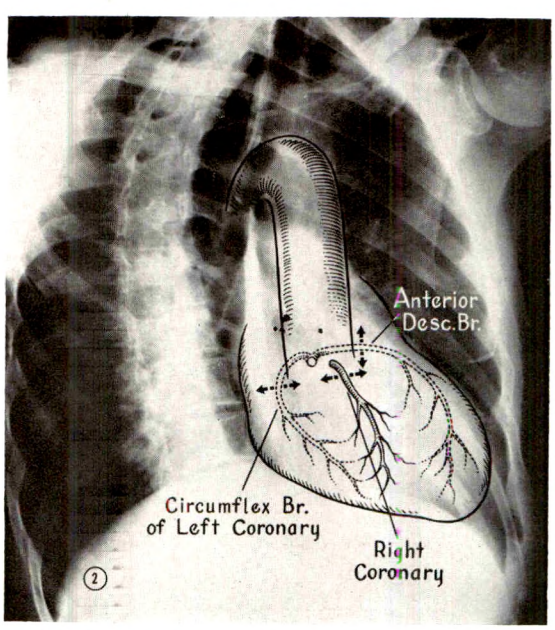


Fig. 2. Right anterior oblique view showing the position and movement of the coronary arteries.

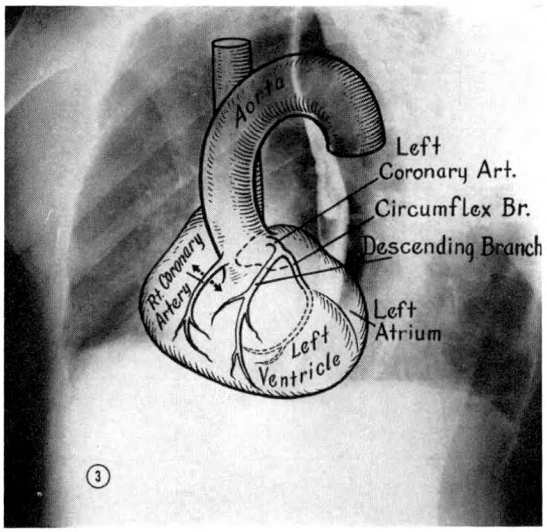


FIG. 3. Left anterior oblique view showing the position and movement of the coronary arteries.

(83 per cent) with all three major branches calcified carry a clinical diagnosis of arteriosclerotic heart disease (in contrast to an over-all arteriosclerotic heart disease incidence of 58 per cent in the 150 patients with coronary calcium), but these 13 patients also had an infarct incidence of 50 per cent (in contrast to an over-all infarct percentage of 30.7 in the 150 patient group). This observation could represent an important factor in the individual prognostication of the risk of arteriosclerotic heart disease and myocardial infarction when using cinefluorography as a screening method.

The left anterior descending coronary artery was found to be the most commonly calcified branch (Table v), which agrees with autopsy studies.[3,12,15]

Autopsy studies shown in Table vi indicate that 13 of 15 patients with coronary calcium seen at cinefluorography had moderate to severe atherosclerosis of the coronary arteries. Of the remaining 2 patients, one had mild coronary sclerosis while the other had normal coronary arteries but had calcification and stenosis of the aortic valve. This last case probably represents either an error in locating the calcium on the part of the radiologists, or a negative error on the part of the pathologist.

Most of the patients in whom moderate to severe coronary atheromatosis was found at autopsy also had marked narrowing of one or more coronary branches. Ten of the 13 patients had localized or diffuse myocardial fibrosis. Ten also had cardiac enlargement of various degrees which apparently did not interfere with the detection of coronary calcium at cinefluorography.

A recent pathologic study of 667 postmortem hearts of individuals, fifteen years of age and older at a New York State hospital, also revealed a relationship between the presence of coronary artery calcification and myocardial infarction, as well as increasing probability of infarction with an increase in the number of coronary arteries calcified.[14]

To further attest to the accuracy of cine-

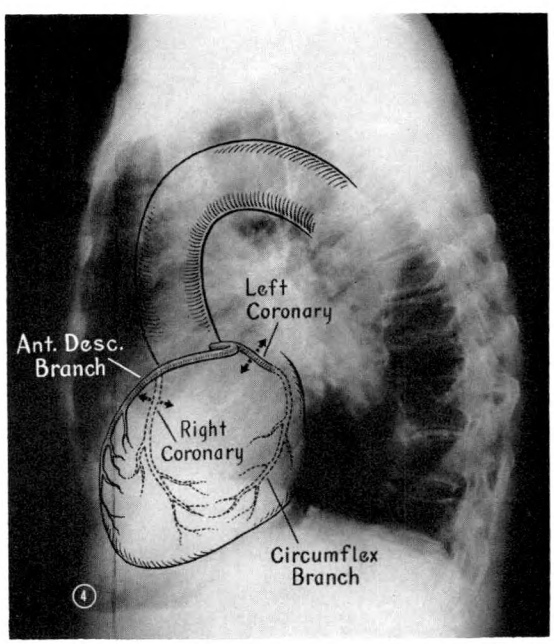


FIG. 4. Left lateral view showing the position and movement of the coronary arteries. The right coronary artery is usually anterior to the anterior descending branch of the left coronary artery in the left lateral view. In the case illustrated here an abnormally large left ventricle displaces the left coronary branch anteriorly.

fluorography in detecting coronary artery disease. 5 of 6 patients (Table VII) with known or suspected heart disease but with no calcium revealed at cinefluorography were found to have normal coronary arteries and myocardium at autopsy. In only one patient was severe coronary atherosclerosis observed at necropsy which could not be detected during cinefluorography of the heart *in vivo* even after review of the cinefluorogram. However, generalized cardiomegaly was present in this patient.

We plan to follow those patients in this study in whom coronary calcification was revealed at cinefluorography but who, as yet, do not exhibit the signs and symptoms of ischemic heart disease. We will then compare them with a similar group of patients without demonstrable coronary calcification with respect to time and manner of onset of clinical arteriosclerotic heart disease.

Since coronary arteriography at present is still unsuitable for routine use due to the complexity of the equipment and the hazard to the patient,[2,6] the relatively simple, rapid, and innocuous method of cinefluorography may be the most efficient screening procedure for the detection of potential candidates for arteriosclerotic heart disease at a time when no electrocardiographic changes or signs and symptoms are present to indicate the extent of coronary atherosclerosis.

SUMMARY AND CONCLUSIONS

Carefully carried out cinefluorography of the heart revealed a high number of coronary artery calcifications. Cardiac enlargement did not interfere as much as expected.

Autopsies showed that visualization of coronary calcification on cinefluorograms indicated considerable coronary atherosclerosis.

In one-fourth of a control group of 60 male patients between forty and seventy-nine years without detectable heart disease and one-fourth of a group of patients in the same age bracket with known or suspected heart disease of various types including ischemic heart disease, coronary calcification was revealed at cinefluorography.

Fifty-eight per cent of 150 predominantly male patients with coronary calcium found at cinefluorography had arteriosclerotic heart disease by clinical evaluation as compared with 39 per cent of a comparable group without coronary calcification.

There was a much higher incidence of angina and myocardial infarction in cases where coronary calcium was detected at cinefluorography.

There was a direct relation between the number of major coronary branches calcified as revealed by cinefluorography and the incidence of clinically manifested arteriosclerotic heart disease. Eleven of 13 men with three major branches calcified had signs or symptoms of ischemic heart disease.

There appears to be a high correlation between coronary calcification as detected by cinefluorography and clinically manifested arteriosclerotic heart disease in males if heart disease is evident or suspected.

Although cinefluorographic evidence of coronary calcium *by itself* appears to be unreliable for predicting the presence of symptomatic ischemic heart disease, it may prove to be a good indicator of potential ischemic myocardial disease.

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IDIOPATHIC MYOCARDIAL HYPERTROPHY

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IDIOPATHIC myocardial hypertrophy refers to cardiac enlargement of unknown etiology in relatively young adults. Usually a severe grade of congestive failure is present; however, some cases may present with only minimal signs of failure, while in others the course is dominated by the effects of pulmonary and systemic embolization. By definition, the diagnosis ultimately rests on the exclusion of known cardiac disorders, although it has been shown that a presumptive diagnosis may be suggested from the clinical picture.[8] It is the purpose of this paper to call attention to certain previously undescribed roentgenographic features which are of great aid in the differential diagnosis of this disease.

MATERIAL AND METHODS

An analysis of 21 cases of idiopathic myocardial hypertrophy yielded 13 cases with satisfactory chest roentgenograms.[8] Four new cases were added to the group. Necropsy confirmation was obtained in 7 cases.

Most of the chest roentgenograms available were posteroanterior teleroentgenograms. These were analyzed for cardiac size, specific chamber enlargement, aortic knob size, status of the pulmonary vasculature, and presence or absence of pulmonary infarction. These findings were then compared with the changes seen in patients with known heart disease of various causes.

CLINICAL FINDINGS

The patients ranged in age from twenty-eight to fifty-seven years with a mean age of forty years. Thirteen were males and 4 were females. Nearly all were Negro, but this is true of the general patient population at our institution.

The symptoms and signs of this group of patients are summarized in Table 1. The most common symptom, dyspnea, is related to congestive heart failure. It is not unusual to obtain a history of cardiac enlargement discovered on routine examination several months to years prior to the onset of symptoms. Although mild antecedent upper respiratory infections are frequently recalled, these patients do not usually have fever or active infection when cardiac manifestations develop. Attempts to identify viral agents by serologic or culture methods have been unsuccessful. Alcoholism may be associated with this disease, but the nutritional status is good and avitaminoses are absent.[4] About 30 per cent of the patients die within one year of the onset of symptoms from intractable congestive heart failure or systemic and pulmonary emboli.

Physical examination may demonstrate

TABLE I

CLINICAL FINDINGS IN 17 PATIENTS

Symptoms and Signs	No.	Per Cent
Dyspnea	16	94
Rales	16	94
Hepatomegaly	13	76
Increased Jugular Venous Distention	13	76
Peripheral Edema	13	76
Chest Pain	8	47
Pleural Effusion	8	47
Pulmonary Embolism	8	47
Hemoptysis	7	41
Alcoholism	5	29
Antecedent Upper Respiratory Infections	5	29
Systemic Emboli	5	29
Ascites	4	24
Digitalis Toxicity	4	24
Myocardial Infarction	1	6

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the signs of congestive heart failure, *e.g.*, rales, hepatomegaly, increased jugular venous distention and peripheral edema, or may be completely negative except for cardiac enlargement. The point of maximum impulse is usually diffuse and forceful; it is located outside the midclavicular line. The rhythm is generally a sinus tachycardia, but slows with digitalis therapy. Gallop rhythm is found in about 50 per cent of cases; organic murmurs are not heard.

The electrocardiogram characteristically shows sinus rhythm and signs of left atrial and left ventricular enlargement. Cardiac catheterizations, ballistocardiograms, and pulmonary function tests are consistent with congestive heart failure.[8]

PATHOLOGIC FINDINGS

All 7 autopsied cases showed pancardiac hypertrophy and dilatation. The weights of the hearts ranged from 500 to 960 gm. with a mean of 600 gm. The pericardium was normal in all instances. The coronary arteries were widely patent and no occlusions could be identified. Only one case showed moderate atherosclerosis of the right coronary artery. The cardiac valves were normal except for functional dilatation of the rings. The endocardium was thin and smooth except in 4 cases where it underlay mural thrombi. These thrombi were located in the left ventricle in all cases, and, in addition, in the right ventricle in one case. The aortas were normal or showed minimal patchy atherosclerosis. Neither renal nor systemic vascular abnormalities suggested pre-existing hypertension. Emboli or infarction were distributed as follows: pulmonary, 4 cases; renal, 3 cases; splenic, 2 cases; and mesenteric, 1 case.

Histologic sections of the hearts showed myocardial hypertrophy with nonspecific tissue changes. Interstitial fibrosis was focal in 6 cases and primarily subendocardial in one case. Viral cultures of the heart were negative in the 2 cases in which they were performed.

A full discussion of the pathologic anatomy of idiopathic myocardial hypertrophy has been given by Elster and his associates.[4]

ROENTGENOGRAPHIC FINDINGS

A similar roentgenographic picture was found in over three-quarters of our cases. The findings are summarized in Table II. Left ventricular enlargement predominates. The diastolic overload on the left ventricle results in dilatation and elongation of its outflow tract. Thus, there is displacement of the cardiac apex to the left and downwards.

The right ventricle is moderately dilated. This results in prominence of that portion of the left heart border just above the left ventricle. The relatively normal pulmonary artery segment and the counterclockwise rotation of the heart, caused by the markedly enlarged left ventricle, combine to preserve the "cardiac waist" on the posteroanterior roentgenogram. In the presence of pulmonary infarction with acute cor pulmonale, there is a further increase in the size of the right ventricle and pulmonary artery, and the cardiac waist is obliterated (see Fig. 1, *A* and *B*).

TABLE II

ROENTGENOGRAPHIC FINDINGS IN 17 PATIENTS

	No.	Per Cent
Cardiomegaly	17	100
Aorta		
Hypoplastic	11	65 \ 77%
Normal	2	12 /
Enlarged	4	23
Left Ventricular Hypertrophy	17	100
Left Atrial Size		
Normal	9	53
Minimal increase	6	35
Moderate increase	2	12
Right Ventricular Enlargement	16	94
Right Atrial Enlargement	2	12
Main Pulmonary Artery		
Normal	11	65
Increased size	6	35
Pulmonary Vasculature Increase	6	35
Pulmonary Infarction	4	23
Mesenteric Infarction	1	6

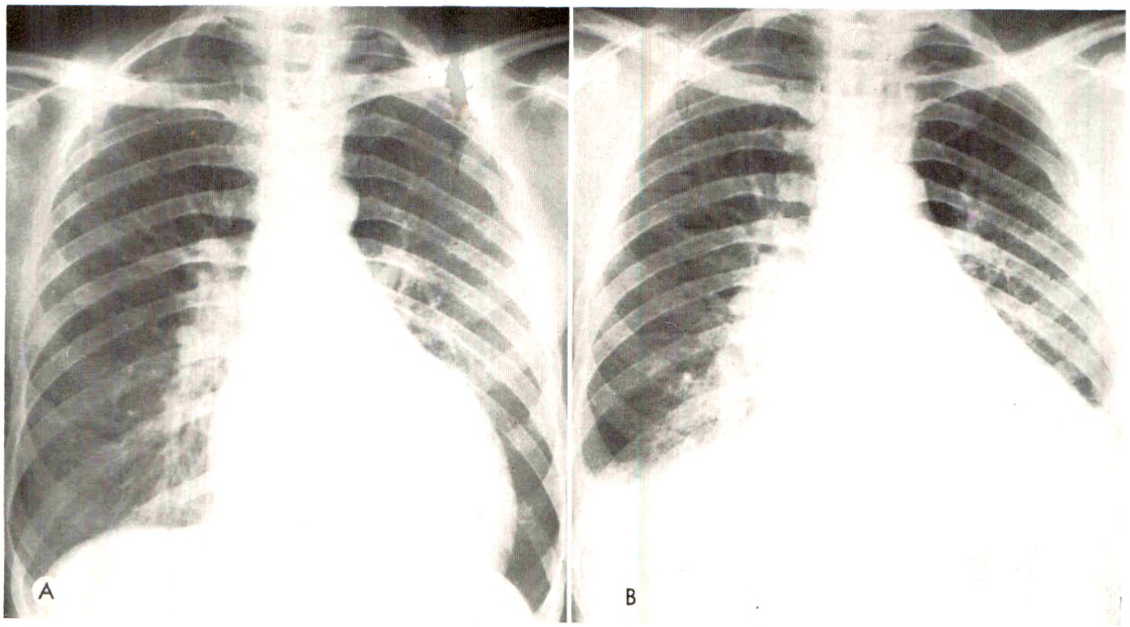


FIG. 1. (*A*) The typical picture of idiopathic myocardial hypertrophy is seen. There is biventricular enlargement and a small aortic knob. Note the preservation of the cardiac waist. (*B*) Same patient as *A*. Pulmonary infarction and acute cor pulmonale with considerable prominence of the pulmonary artery segment and increased right ventricular enlargement.

The left atrium is slightly dilated. Though this was not appreciated on all posteroanterior roentgenograms, the left atrium was seen to be enlarged in all cases of which right anterior oblique roentgenograms with barium in the esophagus were obtained, and in all autopsied cases. The right atrium is also slightly dilated. The cardiac borders are sharply outlined (stenciled heart[2]) due to decreased pulsations of the weakened heart muscle.

The aorta is of normal caliber and the aortic knob appears small relative to the enlarged heart. There is usually no aortic or valvular calcification.* The larger pulmonary arteries are normal; in one-third of the cases they were slightly prominent and were described as top normal. There is no roentgenographic evidence of pulmonary arterial or venous hypertension. The pulmonary veins are normal unless congestive failure or pulmonary infarction supervenes. Pulmonary infarcts were seen in 8 cases.

* Two of our cases showed calcification in the aortic knob. We believe this to be an incidental finding.

Angiocardiograms were performed on 3 patients. There was marked dilatation of the heart, especially of the ventricles. There was pooling of contrast medium on both sides of the heart. This is similar to the pooling and delayed emptying seen in congestive failure. No organic abnormalities were demonstrated.

The following 2 cases were selected to illustrate the characteristic findings of this disease.

REPORT OF CASES

CASE 1. This thirty-nine year old Negro female was admitted to Philadelphia General Hospital in March, 1958 with a fifteen month history of gradually progressing congestive failure, not refractory to therapy. Seven weeks prior to admission she had a transient episode of right hemiparesis and loss of speech lasting two hours.

Physical examination on admission revealed a well nourished female in moderate respiratory distress. The blood pressure was 110/88, respirations 24, pulse 100 and temperature 100.4° F. The neck veins were markedly distended even

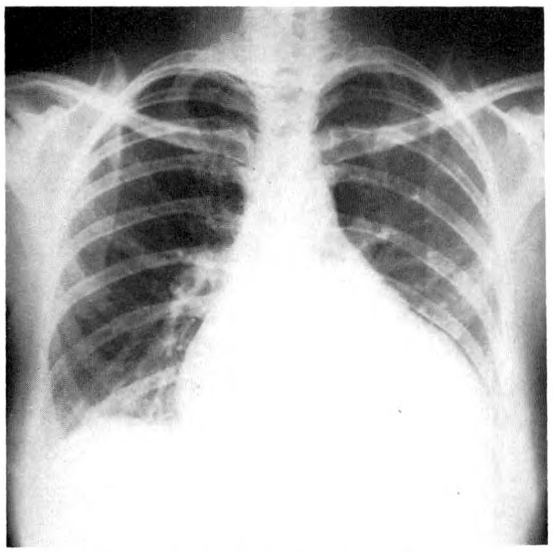


FIG. 2. Case 1. There is biventricular enlargement, fullness of the pulmonary artery segment, and a small aortic knob.

at 90°; a hepatojugular reflux was present. The lungs were clear to percussion and auscultation. The apex beat was at the fifth interspace in the left midaxillary line. There was a grade 3, blowing systolic murmur heard to the left of the sternum in the fourth and fifth interspace which became accentuated with inspiration. There was questionable shifting dullness in the abdomen. A smooth liver edge was palpable 5 cm. below the costal margin. There was 2 plus to 3 plus pitting edema of the legs. No clubbing was noted. Neurologic examination was within normal limits.

Extensive laboratory examinations including urinalysis, complete blood cell count, urea nitrogen, serum proteins, serology, antistreptolysin titer, antihyaluronidase titer, gastric washings for acid fast bacilli, sedimentation rate, gum biopsy, L.E. preparations were essentially negative. All serologic tests for viruses were negative except for the Coxsackie neutralization test which showed titers of 1:8, 1:16 and 1:64 on successive weeks. Electrocardiograms showed atrial disease and biventricular hypertrophy. Roentgenograms of the chest showed a large globular heart (Fig. 2) and the typical findings of a small aortic knob with normal pulmonary vasculature. The venous pressure was 165 mm. H_2O; the circulation time (decholin), 47 seconds. Cardiac catheterization was performed and the findings were consistent with congestive heart failure which persisted despite vigorous therapy and she died on the twenty-sixth hospital day.

The clinical diagnosis was idiopathic myocardial hypertrophy, Coxsackie myocarditis or rheumatic carditis.

Necropsy. The pleural, pericardial and peritoneal cavities were free of abnormal collections of fluid. The heart weighed 500 gm. and was globular in shape. The myocardium was firm, brownish and homogeneous throughout. The papillary muscles were flattened. The endocardium was smooth and transparent, except for an area underlying a mural thrombus in the anterior wall of the left ventricle. This thrombus measured 3×5 cm. and extended from the heart to near the lower margin of the aortic valve. All four cardiac chambers, most notably the left ventricle, were markedly dilated. The valves were thin, delicate and normal in number. The tricuspid orifice admitted three and one-half fingers. The coronary ostia were patent; the coronary vessels were normally distributed, thin-walled and patent throughout. The aorta and its main branches were lined by a smooth intima. The right lung weighed 350 gm., the left 280 gm. The liver weighed 1,410 gm. and was congested. The kidneys showed only old infarcts. No other significant abnormalities were present.

Histologic examination of the heart muscle showed myocardial hypertrophy and focal interstitial fibrosis. The coronary arteries were normal. The lungs showed passive congestion and pulmonary atherosclerosis. Except for several old infarcts, histologic sections of the kidneys were normal. The other organs were unremarkable.

Viral cultures of the heart were negative.

Comment. The rising titer in the Coxsackie neutralization test suggested current virus infection. However, the patient's symptoms and cardiac enlargement started long before these tests were performed. Apparently, the Coxsackie infection was merely an incidental finding in this case. This was borne out by the negative cultures for viruses from the heart muscle and the absence of inflammatory changes.

CASE II. This thirty year old husky Negro laborer was admitted to Philadelphia General Hospital for the first time in September, 1958 because of extreme dyspnea. He stated that he

was in good health until July, 1958 when he noted gradual progressive dyspnea which was incapacitating by September, 1958. He denied prior sore throat, rheumatic fever, hypertension or fever.

Physical examination revealed a well nourished male in acute and chronic respiratory distress. The blood pressure was 110/80, the pulse 120, respirations 32 and temperature 98.6° F. The fundi were normal. The lungs were clear to percussion and auscultation. The left border of the heart was percussed 12 cm. from the midsternal line. The rhythm was rapid and regular. No murmurs were heard, but a presystolic gallop and a paradoxical splitting of the second sound were present. The abdomen was distended and there was questionable shifting dullness. A firm round tender liver edge was palpated 5 cm. below the costal cage. The neurologic examination was within normal limits.

The complete blood cell count, blood sugar and urea nitrogen and serology were normal. The electrocardiogram showed a persistent left bundle branch block, first degree heart block and atrial abnormality. Chest roentgenograms showed right and left chamber enlargement (Fig. 3). Fluoroscopy revealed poor cardiac pulsations. The venous pressure was 130 mm. H_2O and increased to 170 mm. H_2O on hepatic pressure. The circulation time (decholin) was forty-two seconds.

The patient signed out against advice one week later and was readmitted to the Medical Service on October 3, 1958; the physical findings were essentially unchanged. Further laboratory studies included normal liver function tests, protein bound iodine, serum electrolytes and negative L.E. preparations. The patient was given digitalis and diuretics, but still continued to be in respiratory distress. For this reason, extensive pulmonary function tests were carried out and showed the findings associated with cardiac decompensation.

The patient gradually improved with bed rest, but remained dyspneic, with a persistent tachycardia and gallop rhythm. He was discharged after six weeks, but a week later had an exacerbation of his symptoms and was admitted to another institution following a bout of hemoptysis. His condition continued to deteriorate and he died in shock on November 18, 1958.

The clinical diagnosis was idiopathic myocardial hypertrophy.

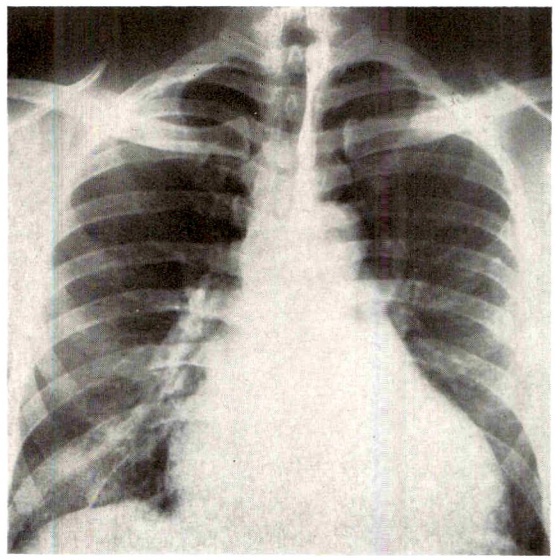


FIG. 3. Case 11. The heart shows the same configuration as in Case 1; however, the aortic knob is normal rather than small.

Necropsy. Permission was granted to examine the heart only. The heart weighed 690 gm. and was greatly dilated. The pericardium and epicardium were normal. The myocardium was firm, reddish brown and homogeneous throughout. Histologic section showed hypertrophy and focal interstitial fibrosis. The endocardium was smooth and transparent. No mural thrombi were present. The valves were normal. The coronary arteries were normal in distribution. The walls of these vessels were smooth and showed no occlusions.

The roentgenograms of 8 additional cases with typical findings are shown in Figure 4, *A–J*, and of 4 other cases with nondiagnostic findings in Figure 5, *A–D*.

ROENTGENOGRAPHIC DIFFERENTIAL DIAGNOSIS

Pericardial effusion is the most difficult and important differential diagnosis that must be made.[2,5,10] There have been several cases reported wherein pericardiocenteses were attempted on patients with idiopathic myocardial hypertrophy. Diffuse enlargement of the cardiac shadow with no venous congestion, sharply outlined heart borders, and decreased to absent cardiac pulsations fluoroscopically are common to both idio-

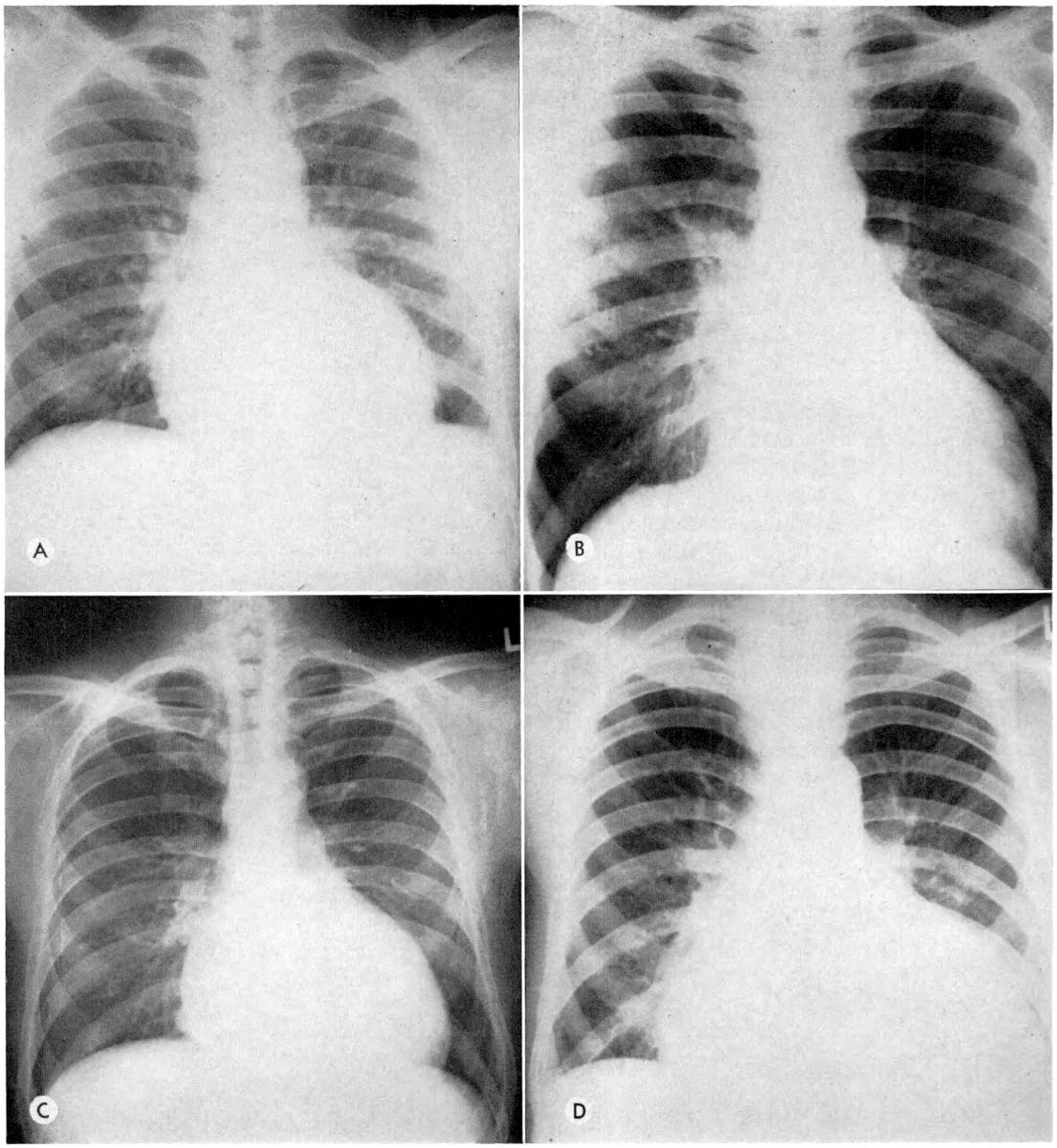


FIG. 4. (*A–D*) These cases show the fairly typical cardiac silhouette seen on the posteroanterior chest roentgenogram. Note the biventricular enlargement with left ventricular predominance. The heart outline is very sharp. Despite the fullness of the pulmonary artery segment, the cardiac waist is still somewhat preserved. The aortic knob is small. The pulmonary vasculature is normal. *C* shows one of the 2 cases with calcification in the aortic knob.

pathic myocardial hypertrophy and pericardial effusion. In pericardial effusion the cardiac waist may be quite broad and there is frequently a loss of the angle made by the shadow of the descending aorta crossing behind the left heart border (Fig. 6). In moderate sized effusions, the normally acute right cardiodiaphragmatic angle becomes obtuse. As the effusion increases, the pericardium bulges laterally beyond its diaphragmatic attachment and the angle again becomes acute. In cardiac dilatation

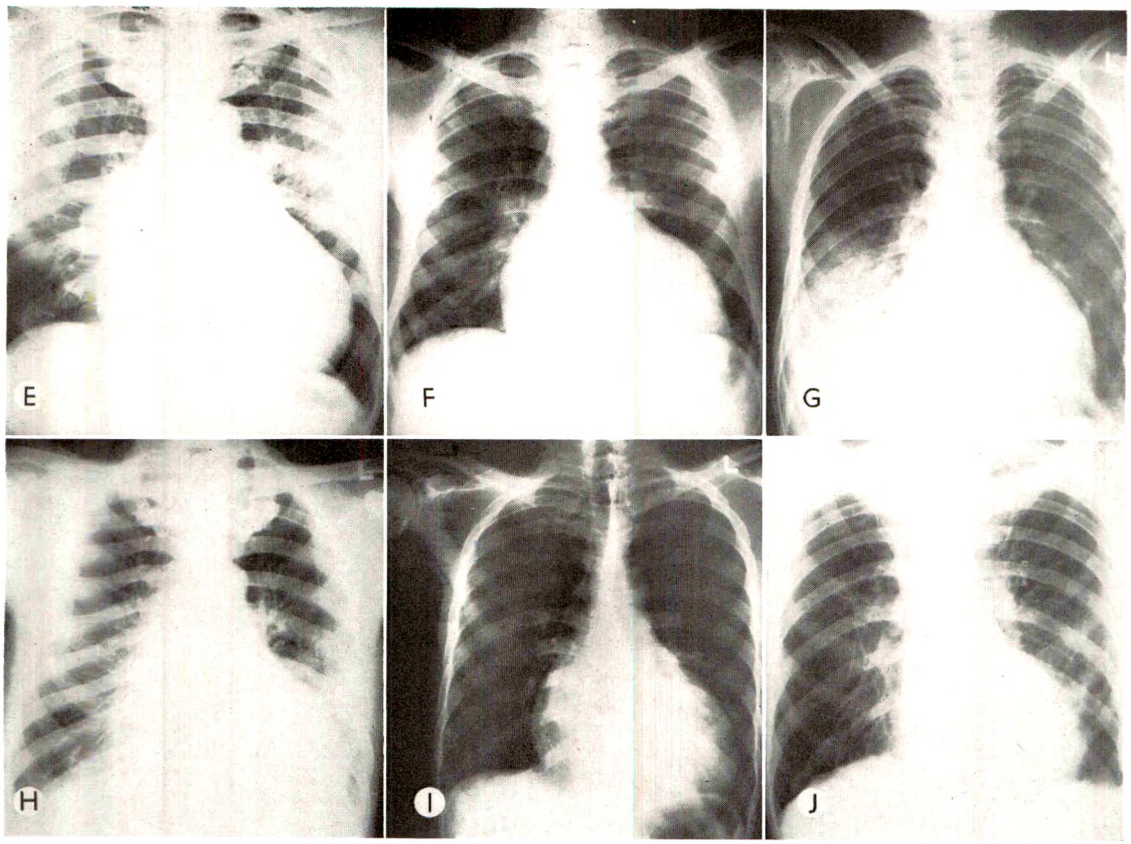


Fig. 4. (*E–J*) Additional cases showing similar changes.

the angle becomes progressively more acute, as it does in large effusions, but it never becomes obtuse. In tuberculous pericardial effusion and myxedema pericardial effusion, the fluid frequently does not extend up to the base of the heart. This may be due to tuberculous adhesions and the viscid character of myxedema effusions. In any effusion where the base of the heart is not involved, it may be impossible to differentiate cardiac dilatation from pericardial effusion on the plain roentgenograms or by fluoroscopic examination (Fig. 7). Where differentiation may be in doubt, angiocardiography is diagnostic. The visualization of a widened pericardial-myocardial shadow between the contrast medium in the right atrium and the outer cardiac border is essentially diagnostic of pericardial effusion.

In pericarditis without effusion the heart is usually small. Pericardial calcification is common in tuberculous pericarditis. Cardiac catheterization reveals a characteristic pressure curve.

Hypertensive cardiovascular disease is probably the most common cause of an enlarged cardiac silhouette in this age group.[5] The diagnosis is usually obvious clinically. However, the "burned out" hypertensive may be clinically indistinguishable from the patient with idiopathic myocardial hypertrophy unless some residual fundoscopic changes are present. Definitive diagnosis is important from the prognostic point of view. The small or relatively small aortic knob of idiopathic myocardial hypertrophy is in marked contrast to the prominent aortic knob seen in hypertensives. In hypertension the left ventricle is the only chamber to enlarge initially. The right ventricle and left atrium enlarge quite

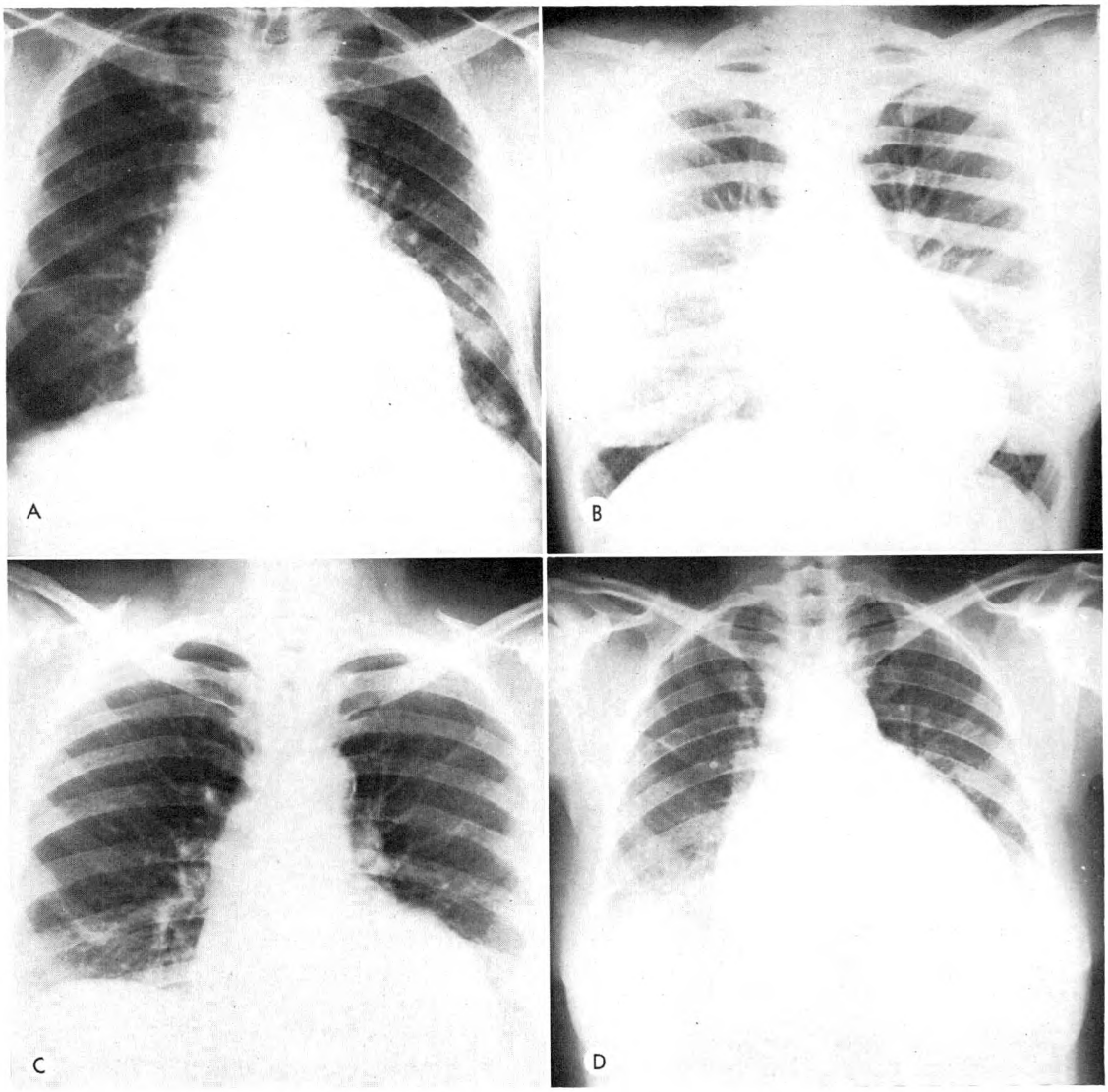


FIG. 5. These are cases with atypical nondiagnostic roentgenographic findings. (*A*) The aortic knob is enlarged in proportion to the left ventricle. (*B*) The right ventricle is larger than usually seen; however, the aortic knob is small. (*C*) This is one of the cases which showed arteriosclerotic changes. Note the aortic calcification. (*D*) The right ventricle is usually prominent. The aortic knob is normal.

late in the course of the disease (Fig. 8). Fluoroscopically the hypertensive heart will exhibit normal or increased pulsations until late when the dilated and weakened heart shows decreased pulsation.

Myocarditis may give a roentgen picture indistinguishable from idiopathic myocardial hypertrophy. However, these patients are febrile and toxic. Electrocardiographic changes may help separate these entities.[9]

Collagen vascular diseases may cause enlargement of the cardiac silhouette. Lupus erythematosus does so by pericardial effusion, and the cardiac findings are no different from those of other effusions. Scleroderma is the only other significant differential diagnosis in this group. The heart is commonly enlarged. Pulsations may be diminished due to collagenous involvement of the myocardium. The pulmonary artery segment is prominent in

patients with extensive pulmonary fibrosis or bronchiectasis.[6] There is usually involvement of many organ systems. The widespread stigmata of scleroderma are in such contrast to the local heart disease of idiopathic myocardial hypertrophy that the differential diagnosis is only rarely a problem.

Cardiac amyloidosis may also present with repeated bouts of congestive failure, frequently of an intractable nature. It usually recurs at an older age group (fifty–sixty years). These hearts are rarely as large as the hearts of idiopathic myocardial hypertrophy.[2] Atrial arrythmias are frequent.[2] Gum biopsies and serum protein analysis may help in the differentiation.

DISCUSSION

Idiopathic myocardial hypertrophy is an eventually fatal disease of unknown etiology occurring in young adults. It is far more common than the few reports in the literature indicate. Discussions with colleagues at other institutions reveal that this entity is being recognized with increasing frequency.

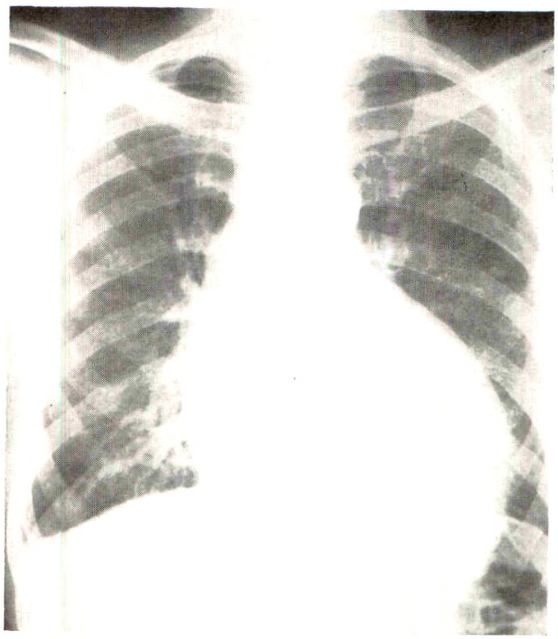


FIG. 7. Tuberculous pericardial effusion. The base of the heart is frequently spared due to pericardial adhesions preventing the movement of fluid. The cardiac configuration is identical with that seen in idiopathic myocardial hypertrophy.

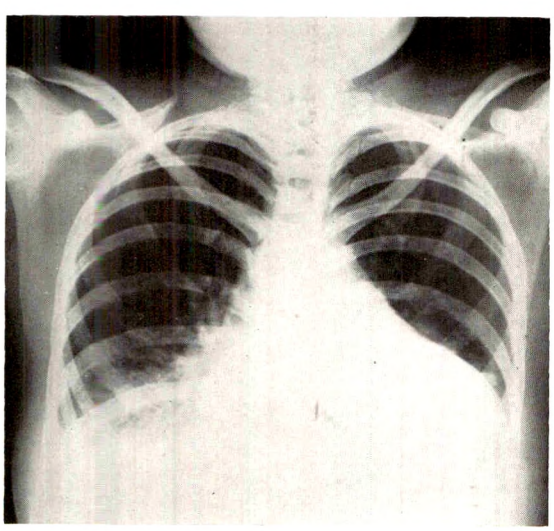


FIG. 6. Pericardial effusion. The cardiac shadow is enlarged and sharply outlined. The enlargement is diffuse. Note how the pericardial fluid has obliterated the normally sharp angle made by the shadow of the descending aorta crossing the left heart border. The right cardiophrenic angle is less acute than one would expect in cardiac dilatation.

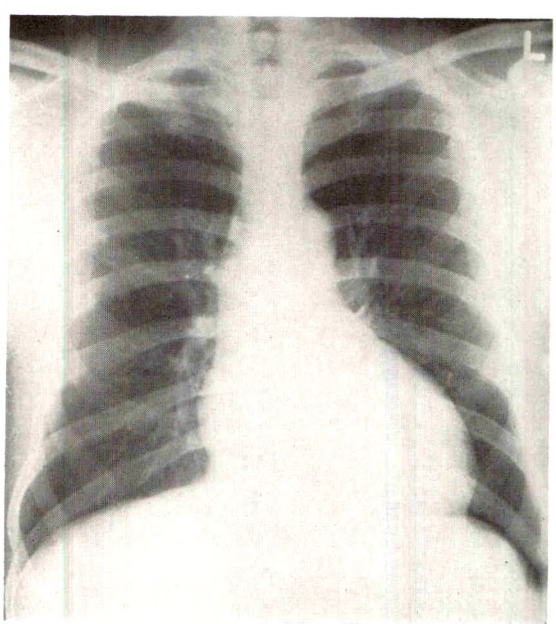


FIG. 8. Hypertensive cardiovascular disease. The left ventricle is enlarged selectively. The aortic knob is prominent and is in proportion to the enlarged left ventricle.

The roentgenographic picture is that of a sharply outlined heart with diffuse ventricular dilatation (left ventricular enlargement predominating), mild left atrial enlargement, occasional right atrial enlargement, a small aorta and somewhat prominent major pulmonary arteries. The frequency of pulmonary and systemic embolization is such that the combination of a cardiac silhouette as described above and pulmonary or mesenteric infarction occurring in a relatively young adult should make one strongly suspect idiopathic myocardial hypertrophy.

When pericardial effusion is a prime consideration, angiocardiography can be diagnostic.

SUMMARY

The clinical, pathologic and roentgenographic findings of idiopathic myocardial hypertrophy are presented with emphasis on the roentgenographic aspects. Two typical cases are included.

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STAPHYLOCOCCAL PNEUMONIA IN ADULTS*

A REVIEW OF 102 CASES

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BECAUSE of the paucity and variance of reported cases (a total of 88 cases in four of the largest series in the literature)[3,5,6,9] of a serious disease of rapidly increasing frequency, the cases of staphylococcal pneumonia in adults seen at Wadsworth Veterans Administration Hospital during a seven year period (1953–1959) were reviewed. Table 1 compares our findings with those in four other adult series and in one large series composed of children. The 102 cases reported here represent approximately half of the total cases admitted; the remainder could not be reported because of the loss or transfer of charts and roentgenograms.

MATERIAL

All patients were male, ranging from eighteen to eighty-two years of age (79 per cent were fifty-five years or older). Hemolytic coagulase positive staphylococci were

TABLE I

MORTALITY AND CALCULATIONS OF STAPHYLOCOCCAL PNEUMONIA

Author	No. of Cases	Mortality (per cent)	Lung Abscess (per cent)	Empyema (per cent)	Pneumatocele (per cent)	Effusion (per cent)	Pneumothorax (per cent)	Bronchopleural fistula (per cent)	Atelectasis (per) cent)
In Adults									
Present Series	102 (1953–1959)	60.5	24.5	7.8	1	37.2	0	0	21.6
Ede *et al.*[3]	36 (1956–1958)	2.8	8	27.7	3.6	22	25	25†	NA
Fisher *et al.*[5]	21 (1942–1957)	67	43*	19	NA	NA	NA	NA	NA
Gold and Davis[6]	13 (1957–1958)	15.4	23	0	NA	23	NA	NA	NA
Hausmann and Karlish[9]	18 (1952–1954)	0	27	11	NA	NA	5.5	5.5	NA
In Children									
Rebhan and Edwards[16]	329 (1950–1958)	14.3	21	8.8	NA	NA	41	3.7	NA
	(Present on admission)		(7)	(NA)	(6.2)	(55)	(21)	(0)	(15.2)

* 10 cases came to postmortems; 9 had lung abscess.
† Reported as pyopneumothorax.
NA—Figures not available.

* From Wadsworth Hospital, Department of Radiology, Veterans Administration Center and the Department of Radiology, University of California at Los Angeles, Medical Center, Los Angeles, California.

cultured in all patients from the following sources: sputum, 90 per cent; blood, 23.5 per cent; pleural effusion, 6.8 per cent; bronchi, 6.8 per cent; lung abscess, 4.9 per cent. Cases of both primary pneumonia (83 cases) and secondary pneumonia (15 cases), *i.e.*, those with previous or coexisting staphylococcal infection elsewhere in the body, were included in the series, with 4 classified as uncertain as to type. The marginal punch card system of recording data was used.

INCIDENCE

Prior to 1950 very few cases of adult staphylococcal pneumonia unassociated with an influenza epidemic were reported. In more recent literature, cases of staphylococcal pneumonia in infants are legion; however, the authors reporting on adult staphylococcal pneumonia infer that this is a relatively rare disease. In recent years there has been a rapidly increasing incidence. In our series, 52 per cent of the cases occurred in 1959.

PREDISPOSING FACTORS

Gresham and Gleeson-White[7,8] feel that alveolar edema may be the common denominator in a host of conditions that predispose a person to staphylococcal pneumonia: chronic lung or heart disease, coma, influenza, suppression of the cough reflex postoperatively, and old age and debilitation. Others agree that staphylococcal pneumonia is a major problem in patients with a pre-existing complicating disease, and that when it does occur in these patients it is more likely to be fatal. This seems to be true, indeed, as 88 per cent of our cases had complicating diseases and the mortality rate was 65.5 per cent, whereas in uncomplicated cases the mortality rate was 25 per cent. Of those with complicating disease, 64.5 per cent had chronic lung or cardiovascular disease and 22 per cent had malignancies. Other complications of lesser frequency were: cirrhosis, diabetes, coma, uremia from chronic renal disease, blood dyscrasias, and general debility. Only those cases with a significant titer were considered to have had influenza; of these there were 2. The *Staphylococcus* as an opportunist invader now has the role previously played by the pneumococci in terminal infection.

Similarly, those patients who have recently received antibiotics or steroids prior to the development of pneumonia, as well as those patients who develop staphylococcal pneumonia while in the hospital (*i.e.*, acquire a hospital organism), are generally agreed to be more prone to develop a more serious and fatal form of the disease. The mortality rate was 72.5 per cent in 29 patients who had recent prior treatment with antibiotics, and 83 per cent in 6 patients who developed staphylococcal pneumonia while on steroids. The majority of our cases (55 per cent) developed pneumonia in the hospital. The mortality rate in this group was 71.5 per cent as compared to 53.5 per cent in that group which presented with pneumonia on admission. When pneumonia develops in a hospitalized patient who is on steroids or antibiotics, it should be considered staphylococcal until proved otherwise.

CLINICAL FEATURES

The clinical pattern of staphylococcal diseases is apparently changing in all age groups, although staphylococcal pneumonia is a more protean disease in adults than in children, who still present a rather characteristic picture. Gresham[8] reports one extreme when he describes a different clinical and pathologic picture which is being seen in adult patients: sudden onset, rapid deterioration, a short course, and hemorrhagic consolidation, or a course similar to the classic description by Chickering and Park[2] of patients developing staphylococcal pneumonia as a complication of influenza. On the other hand, others describe a disease of insidious onset, prolonged course, and a high incidence of complications. Figures 1 and 2 show the type of onset, duration, and mortality for the present series. Although no striking

characteristic clinical pattern was noted in reviewing our cases, the fulminating form of pneumonia was more frequent in the last two years of the study as compared to the earlier years.

The radiologist should be aware of the variable nature of this disease regarding the roentgen findings; they may be present prior to clinical onset or may be completely lacking or minimal, appearing several days later in a severely ill patient. He should be especially conscious of the fulminating type of this disease in which the clinical history of sudden onset and rapid deterioration may lead to the false diagnosis of pulmonary embolism, particularly in the postoperative patient, who not infrequently develops this complication.[11] (Sixteen cases in this series developed staphylococcal pneumonia within a fifteen day postoperative period.)

ROENTGEN FINDINGS

Roentgen examination quite frequently suggests the diagnosis of staphylococcal pneumonia in children because of the extensive and characteristic findings, particularly pneumatoceles and pneumothorax, present on admission. (See Table 1 for

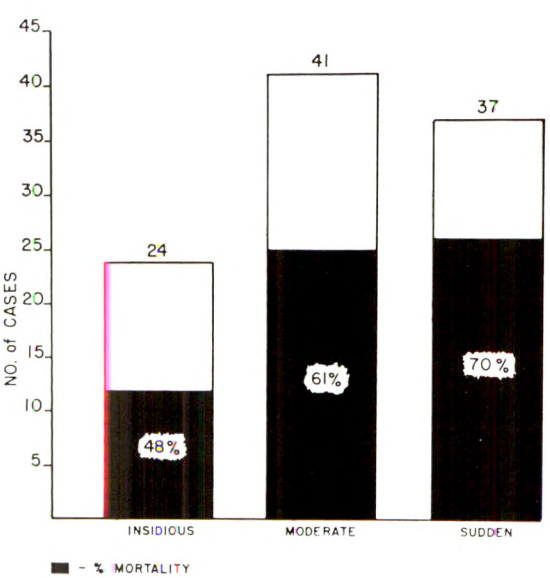


FIG. 1. Type of onset and mortality.

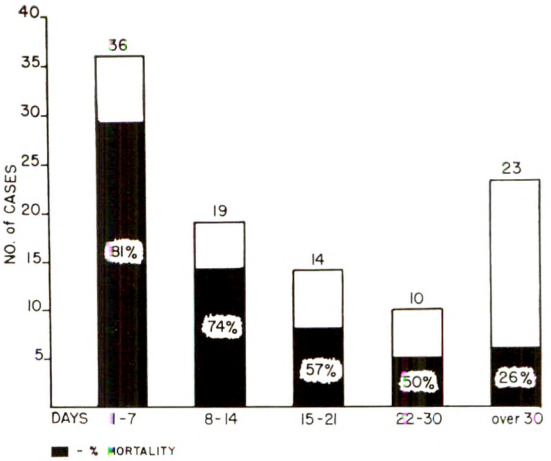


FIG. 2. Duration and mortality.

Rebhan and Edwards'[15] findings in children.) Adults, on the other hand, usually present with a nonspecific pneumonic infiltration which, in the majority of cases, becomes a bronchopneumonia indistinguishable from any other type of bronchopneumonia, except for the rapidly changing roentgen findings (Fig. 3, *A* and *B*) and the development of pleural effusion, which occurs much more commonly (37.2 per cent) than in streptococcal or pneumococcal pneumonia. In this present series, 98 per cent of the cases had bronchopneumonic infiltrates which were usually bilateral (68.5 per cent) (Fig. 4) and rarely segmental (4 per cent) in distribution. Regarding the amount of lung tissue involved, 59.5 per cent had diffuse involvement.

Frequent roentgen studies are necessary in following this disease because of the rapid change with new areas of involvement (Fig. 3, *A* and *B*). This was seen in 54 per cent of our cases at some time during the course.

The patient should not be discharged until his chest roentgenogram is completely clear. Six patients in this series who were clinically well were discharged before the chest roentgenogram showed complete resolution; all were readmitted with exacerbation of pneumonia within one to four weeks.

The development of pneumatoceles and



FIG. 3. Rapidly changing roentgen findings. (*A*) March 4, 1957: left upper lobe involvement; (*B*) March 6, 1957: moderate clearing on the left with the development of right upper lobe involvement within two days.

pneumothorax, so characteristic of staphylococcal pneumonia in infants, is rare indeed in adults. Only 1 case had pneumatocele formation and there were no cases of pneumothorax. Because of the lack of distinctive features, except those mentioned above, the radiologist's most important function is the early recognition of complications most common in adults—lung abscess and empyema—and following their course.

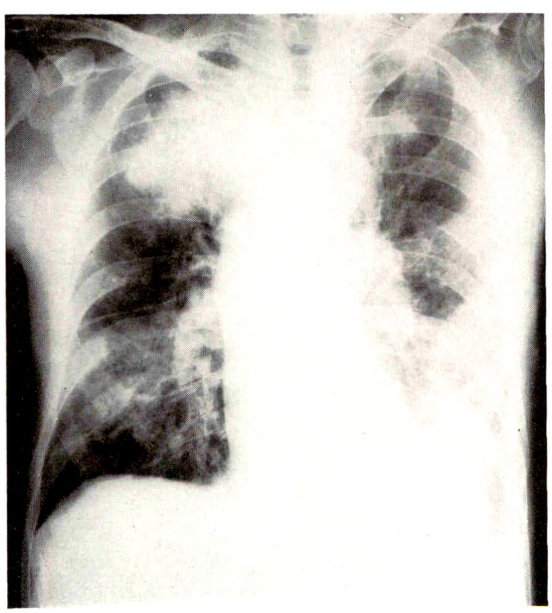


FIG. 4. Typical roentgen findings. October 12, 1957: bilateral bronchopneumonia with multiple sites of involvement.

LUNG ABSCESS

The ability of the *Staphylococcus* to create lung abscesses is primarily due to its exotoxins, which apparently have a dual action: (1) production of vasculitis and paralytic dilatation of capillaries and venules, and (2) a direct necrotizing effect on lung parenchyma.[10]

Meyers and Jacobson[13] state that "true lung abscesses occur more frequently in adults than in children." A comparison of this present series with that of Rebhan's and Edwards[15] indicates only a slightly higher incidence (3.5 per cent) in adults.

Ede *et al.*[3] report that "infiltrates which persist will usually demonstrate cavity formation within ninety-six hours." Rapid

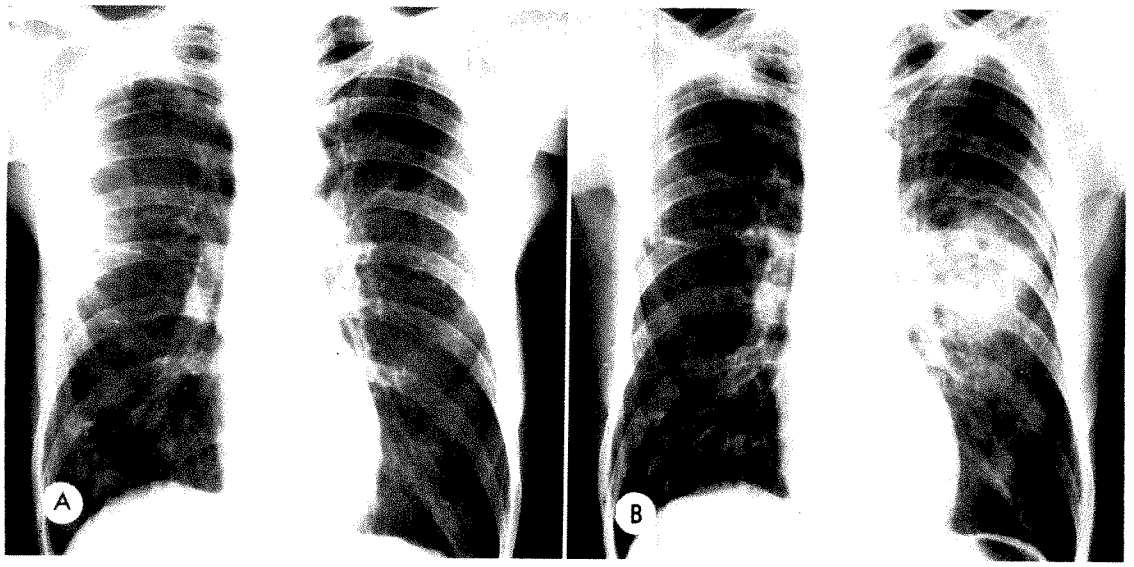


FIG. 5. Rapid development of cavitation. (*A*) October 23, 1959: left lung clear; (*B*) October 26, 1959: multiple cavitations developing in three days.

cavity formation (Fig. 5, *A* and *B*) occurred in approximately one third of our 25 cases of lung abscess (Fig. 6). However, this complication also appeared in some patients after they had had pneumonia roentgenographically demonstrated for over a month (Fig. 7, *A–D*). Figure 8 indicates the roentgenologic duration of cavities once they appeared, usually at least four to six weeks in those patients surviving.

Brock states that the posterior segment of the right upper lobe is the area most frequently involved in staphylococcal lung abscesses. Our random distribution did not bear this out. In cases of secondary pneumonia, *i.e.*, vascular embolism, there seems to be a predilection for the lower lobes, possibly due to the straighter course of the blood vessels. In addition, in cases of both primary and secondary pneumonia, multiple cavities were the rule. Bronchogenic spread undoubtedly accounts for the multiplicity. The same patient may have all phases of development and healing going on at the same time.

The characteristic "soap bubble" appearance of staphylococcal cavities described by Brock[1] was not encountered in our series. By far the greatest number of our cases (72 per cent) had thick and sometimes shaggy cavity walls.

Not only morbidity but also mortality (71 per cent) was higher in patients developing this complication. Indeed, the patient's life is in jeopardy until the lung abscess is roentgenologically demonstrated as being completely healed.

EMPYEMA

Empyema, the second most common complication (7.8 per cent) in our series,

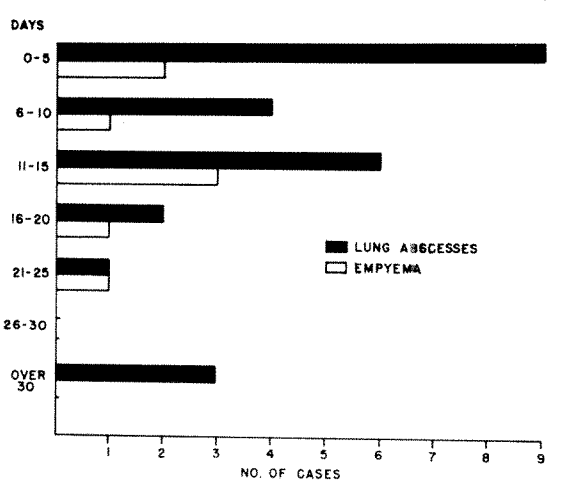


FIG. 6. Length of time between the onset of pneumonia and the development of complications.

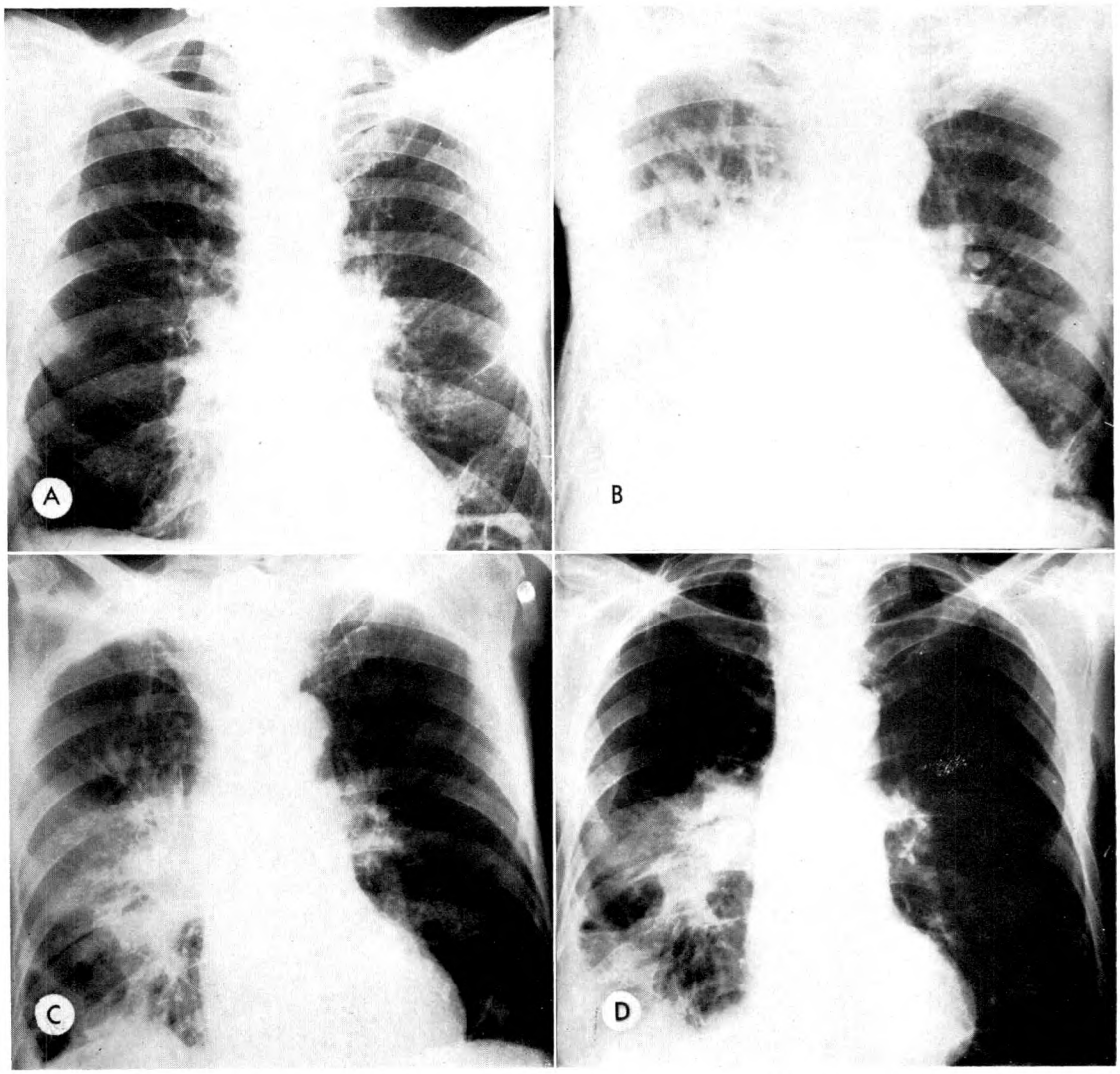


FIG. 7. Late development of cavitation. (*A*) February 8, 1959: minimal findings on the right; (*B*) February 11, 1959: rapid consolidation; (*C*) March 23, 1959: persisting infiltration; (*D*) April 14, 1959: late cavitation after five weeks.

may develop by rupture of a lung abscess, direct extension from the lung via the lymphatics, septic embolization, or contamination during thoracentesis for pleural effusion. Instances of all except the first (rupture of an abscess) were seen in our cases.

Figure 6 indicates the length of time between the onset of pneumonia and the development of empyema; Figure 8 indicates the roentgenologic duration; and Figure 9, *A* and *B* shows the characteristic roentgen findings. Although the length of hospitalization and the morbidity are appalling, this appears to be in adults a less serious complication than lung abscess with regard to mortality (25 per cent). In children, on the other hand, empyema is much more serious, with a mortality rate of 50 to 70 per cent.

All of our cases of empyema were treated by surgical drainage. Before effective drainage can be instituted, exact roentgen localization is necessary. This can be done in

most instances by plain roentgenography though, in low lying empyemas intimately associated with the diaphragm, injection of the empyema with contrast material prior to surgical drainage is important in order to avoid inadvertent puncture of the diaphragm with resultant subphrenic abscess.

In those cases where plain roentgenography is sufficient for localization, once drainage is established, the volume, extent and shape of the affected area can be determined by injecting aqueous dionosil or other suitable contrast media (Fig. 10, *A* and *B*). The volumetric studies thereafter can be performed with sterile saline solution, but the initial examination must be done using a contrast medium and with the patient examined in the erect and decubitus positions to rule out a bronchopleural fistula (Fig. 10 *C*) which, if present, would cause the lung to be flooded if saline solution were injected blindly.[12] Roentgen studies with contrast material are repeated as necessary during the follow-up for two reasons: to rule out the possibility of the development of (1) a bronchopleural fistula, since the empyema will not heal as long as air is supplied to the space, thereby preventing lung expansion, and (2) a blocked off area which, of course, would not drain because of lack of communication.

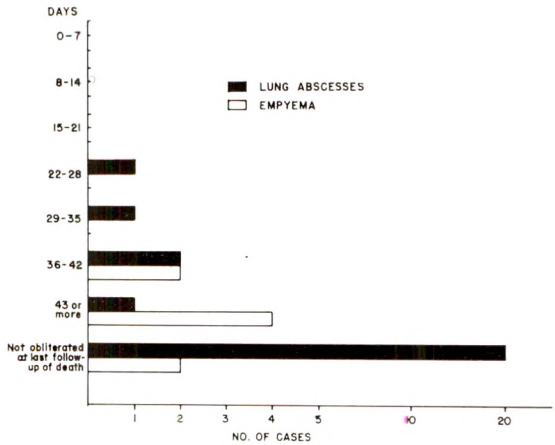


FIG. 8. Roentgenologic duration of complications.

The early roentgen diagnosis of complicating empyema will result in faster healing, since surgical drainage can be instituted before pleural thickening occurs and while the lung can still expand easily.

SUMMARY

A series of 102 cases of staphylococcal pneumonia in adults is reviewed and com-

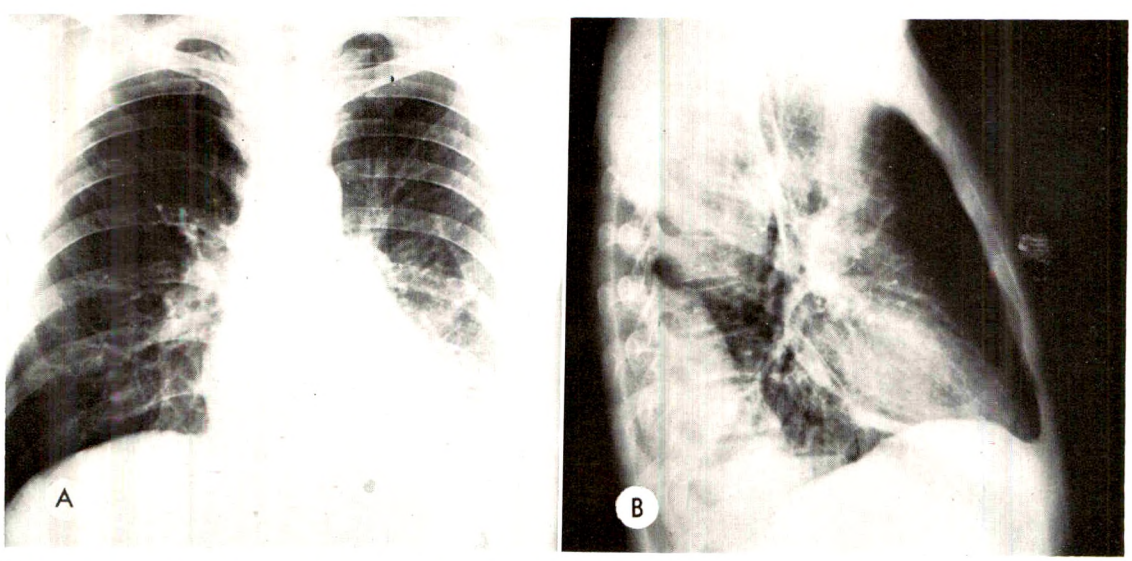


FIG. 9. A case of empyema which developed within one week after the onset of pneumonia and persisted for twelve weeks. (*A* and *B*) December 26, 1957: roentgenograms made midway in the course of the illness show the characteristic roentgen findings.

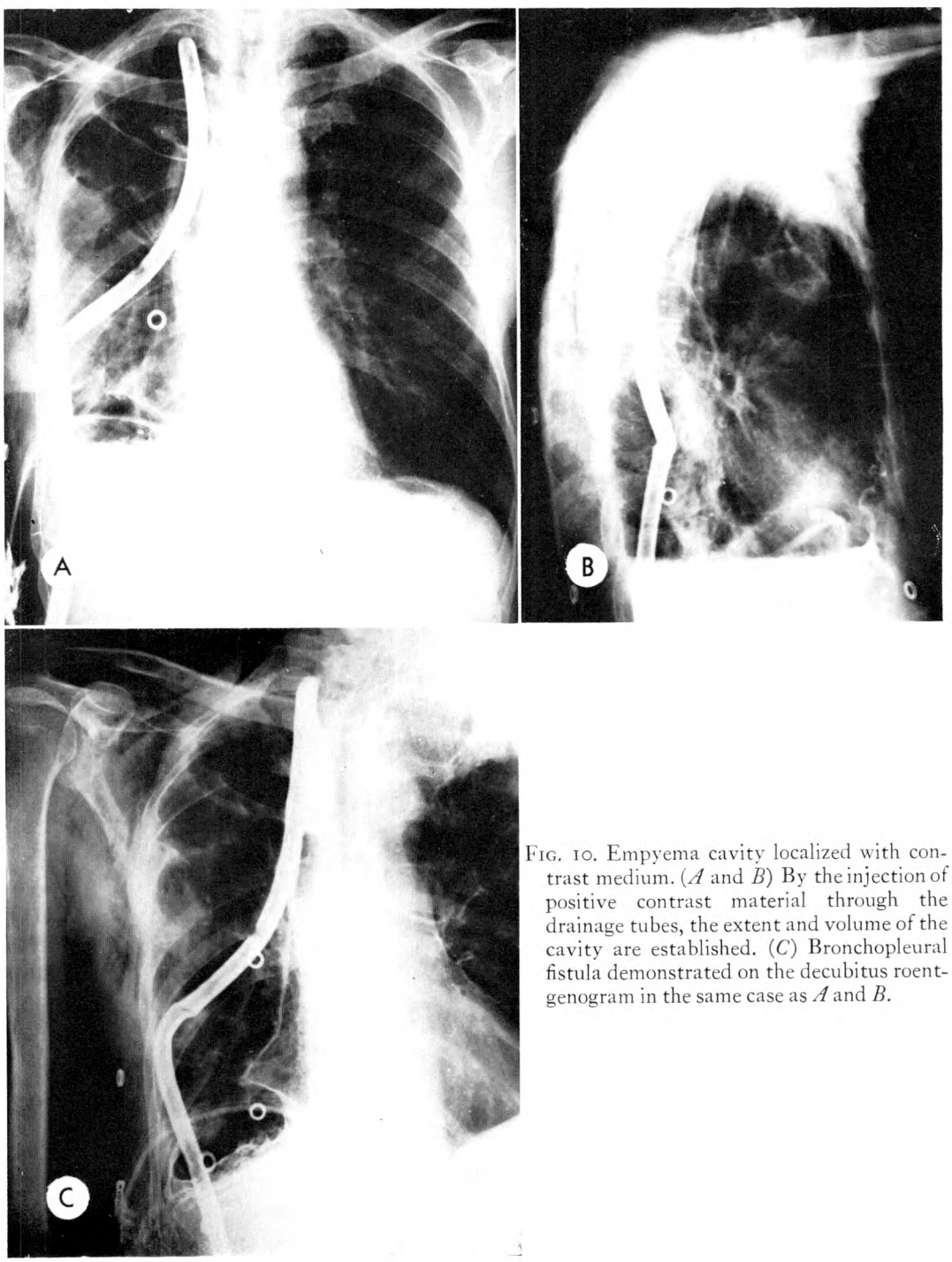


FIG. 10. Empyema cavity localized with contrast medium. (*A* and *B*) By the injection of positive contrast material through the drainage tubes, the extent and volume of the cavity are established. (*C*) Bronchopleural fistula demonstrated on the decubitus roentgenogram in the same case as *A* and *B*.

pared with four other series in adults and one large series in children. The increased incidence, protean nature, and clinical pattern of this disease are described. Because of the relatively nonspecific early roentgen findings, the radiologist's role in the early recognition, localization, and follow-up of complications cannot be too highly stressed.

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SPONTANEOUS PNEUMOTHORAX AS A COMPLICATION OF PULMONARY METASTASES IN MALIGNANT TUMORS OF CHILDHOOD*

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MANY malignant neoplasms of childhood metastasize to the lungs, a variety of secondary effects resulting from their presence. Such manifestations as bloody pleural effusion and compression atelectasis are common, but the development of spontaneous pneumothorax is not often encountered. De Barrin[4] was the first to report the occurrence of spontaneous pneumothorax in a patient with metastatic tumor in the lungs. Including the case reported by him, there have been 29 instances of this complication recorded in the literature.[1–8,10–17] Thirteen additional such patients have been seen at The Children's Hospital and the Children's Cancer Research Foundation (Table I).

The primary tumors implicated in the cases heretofore reported were: osteogenic sarcoma, 9 patients; Ewing's tumor, 5 patients; "carcinoma" (type not specified), 3 patients; leiomyosarcoma, adenocarcinoma, and fibrosarcoma, 2 patients each; renal cell carcinoma, adrenal carcinoma, angiosarcoma, rhabdomyosarcoma, Wilms' tumor (adult type), and carcinoma "à cellules acidophiles," 1 patient each. Of these 29 patients, 7 of the 8 who were sixteen years of age or younger on whom sufficient information was supplied were found to have primary tumors in bone (Table II). The experience at this institution has been similar. Nine of the 13 patients with spontaneous pneumothorax had malignant neoplasms of bone.

In order to investigate this apparent association further, the records of the X-ray Therapy section were reviewed. The

TABLE I

CHILDREN WITH SPONTANEOUS PNEUMOTHORAX COMPLICATING PULMONARY METASTASES
AUTHORS' SERIES

Case		Sex	Age (yr.)	Type of Tumor	Site of Primary Tumor	Site of Pneumothorax
1	R.B.	M	16	Osteogenic sarcoma	Left femur	Right
2	B.H.	F	14	Osteogenic sarcoma	Left femur	Bilateral
3	J.P.	M	13	Osteogenic sarcoma	Left tibia	Bilateral
4	M.E.	F	13	Osteogenic sarcoma	Right tibia	Left
5	R.M.	M	11	Osteogenic sarcoma	Right femur	Right
6	B.S.	M	10	Osteogenic sarcoma	Right humerus	Left
7	L.F.	F	9	Osteogenic sarcoma	Left ilium	Bilateral
8	S.B.	F	10	Ewing's tumor	Left fibula	Right
9	M.O.	F	9	Ewing's tumor	Left humerus	Right
10	M.N.	F	6	Wilms' tumor	Left kidney	Left
11	T.S.	M	5	Wilms' tumor	Left kidney	Right
12	M.DeM.	F	5	Wilms' tumor	Left kidney	Left
13	M.C.	F	11	Hemangioendotheliosarcoma	Left thigh	Right

* From the Department of Radiology and The Children's Cancer Research Foundation, The Children's Hospital Medical Center; and the Department of Radiology, Harvard Medical School, Boston, Massachusetts.
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Table II

CHILDREN WITH SPONTANEOUS PNEUMOTHORAX COMPLICATING PULMONARY METASTASES
CASES FROM THE LITERATURE

Authors	Sex	Age (yr.)	Type of Tumor	Site of Primary Tumor	Site of Pneumothorax
De Barrin[4] (1937)	M	15	Fibroblastic sarcoma	Left pubic bone	Left
Christmann *et al.*[2] (1950)	M	12	Ewing's tumor	Left calcaneus	Right
Leigh and Thompson[7] (1951)	M	11	Osteogenic sarcoma	Right tibia	Right
Sherman and Brant[13] (1954)					
Case 1	M	9	Ewing's tumor	Sacrum	Bilateral
Case 2	M	16	Ewing's tumor	Sacrum	Left
Case 3	F	9	Osteosarcoma	Left tibia	Right
Engle[6] (1958)	F	15	Osteogenic sarcoma	Femur	Bilateral
Torricelli and Canossi[15] (1958)	F	11	"Ewing's tumor"	Soft tissues of left shoulder	Left

ten year period 1948–1957 was selected for detailed study. During this interval, 381 patients less than seventeen years of age with malignant neoplasms received roentgen treatment. Some patients with cancer seen at this hospital are not included in the total since roentgen therapy was not required during the course of their illness. Also not represented are those children with lymphosarcoma in whom acute leukemia became manifest. An additional 121 patients (59 boys and 62 girls) had central nervous system tumors. This group has not been analyzed further since no pulmonary metastases developed in any patient.

The roentgenographic findings of each child were reviewed with special attention to the demonstration of pulmonary metastases and an associated spontaneous pneumothorax. No pneumothorax was considered to be spontaneous if preceded by a thoracentesis on the same side. The results of this analysis, according to diagnosis, are given in Table III. When referring to the table, it should be noted that absence of pulmonary metastases does not necessarily imply eventual survival of the patient. In fact, some of the children in this category died from the effects of local or disseminated disease.

A total of 7 cases of spontaneous pneumothorax associated with pulmonary metastases was encountered in the period under study. This represents 2 per cent of the entire group of 381 children, or 6 per cent of the 125 who developed metastases. Five of these 7 patients had primary bone tumors. Osseous neoplasms account for only 13 per cent of the 381 children and 28 per cent of the patients with pulmonary metastases. This compares with but one child with pneumothorax among the patients with Wilms' tumor, which neoplasm comprises 24 per cent of the total and 35 per cent of those with lung deposits. Children with diagnoses other than those already listed made up 63 per cent of the total and 37 per cent of those with metastases. Only one instance of spontaneous pneumothorax was found in this group.

Since osteogenic sarcoma was the neoplasm encountered most frequently in this connection, all children with this diagnosis who developed pulmonary lesions were studied in detail. The points considered were: age; sex; site of primary tumor; distribution of the pulmonary metastases according to location within the inner, middle or outer third of the lung fields; and the osteoblastic, nonosteoblastic or mixed nature of these deposits. The interval between the onset of disease, the development of pulmonary lesions and the time of death was also investigated. No correlative factor was ascertained; the patients with pneumothorax were similar to those who died

TABLE III

ROENTGENOGRAPHIC INCIDENCE OF PULMONARY METASTASES AND OF PNEUMOTHORAX
SELECTED GROUP OF 381 CHILDREN WITH MALIGNANT TUMORS

Type of Tumor	No. of Cases		No. of Cases with Lung Metastases		No. of Cases with Pneumothorax			
	Total	Sex	Total	Sex		Site		
					Sex	Right	Left	Bilateral
Neuroblastoma	107	M 60 F 47	11	M 7 F 4				
Wilms' tumor	92	M 45 F 47	44	M 20 F 24	M F		1 (Case 10)	
Bone Tumors Osteogenic sarcoma	27	M 12 F 15	19	M 8 F 11	M F	2 (Cases 1, 5)	1 (Case 6)	1 (Case 7)
Ewing's tumor	23	M 14 F 9	15	M 9 F 6	M F	1 (Case 8)		
Reticulum cell sarcoma	1	M 0 F 1	0					
Rhabdomyosarcoma	14	M 11 F 3	2	M 1 F 1				
Teratoma	8	M 4 F 4	5	M 2 F 3				
Hemangioendothelio-sarcoma	7	M 3 F 4	5	M 3 F 2	M F	1 (Case 13)		
Mixed mesodermal tumor	6	M 5 F 1	2	M 2 F 0				
Angiosarcoma	5	M 1 F 4	2	M 0 F 2				
Adenocarcinoma	4	M 3 F 1	0					
Undifferentiated carcinoma	4	M 3 F 1	3	M 3 F 0				
Neurofibrosarcoma	3	M 1 F 2	3	M 1 F 2				
Undifferentiated sarcoma	3	M 2 F 1	1	M 0 F 1				

Table III—(*Continued*)

Type of Tumor	No. of Cases		No. of Cases with Lung Metastases		No. of Cases with Pneumothorax			
	Total	Sex	Total	Sex	Sex	Site		
						Right	Left	Bilateral
Fibrosarcoma	2	M 2 F 0	2	M 2 F 0				
Chondrosarcoma	1	M 1 F 0	1	M 1 F 0				
Miscellaneous carcinomas	14	M 10 F 4	5	M 5 F 0				
Lymphoma and Allied Diseases Lymphosarcoma	19	M 11 F 8	1	M 1 F 0				
Hodgkin's disease	18	M 12 F 6	4	M 2 F 2				
Malignant lymphoma	14	M 13 F 1	0					
Reticulum cell sarcoma (nonosseous)	9	M 4 F 5	0					
Totals	381	M 217 F 164	125	M 67 F 58		4	2	1

with pulmonary metastases but without developing free air in the pleural cavity. However, the impression was gained that in children with osteogenic sarcoma, the first demonstrable pulmonary metastases are frequently located more peripherally than those originating from nonosseous neoplasms. In fact, small subpleural deposits were often the first visible evidence of lung involvement. This distribution may be important in explaining the genesis of pneumothorax in these patients.

Thornton and Bigelow[14] described a young adult with osteogenic sarcoma and spontaneous pneumothorax in whom a bronchopleural fistula was demonstrated at autopsy. The communication resulted from necrosis of a peripheral pulmonary nodule. Lodmell and Capps[8] encountered a patient who exhibited a similar process. In case 3 of our series, two bronchopleural fistulae were found at operation. They extended through friable tumor to the subpleural level where blebs then formed. These in turn ruptured into the pleural cavity (Fig. 1). While there is no doubt regarding the origin of the pneumothorax in this patient, the evidence obtained at autopsy in other children proved more difficult to interpret. Of the 11 patients of this series who died, postmortem examinations were performed in 7. Necrotic neoplastic tissue pouting into the pleural cavity was found in all. Rents could be seen extending deeply into some tumor nodules. These findings could be interpreted as evidence of antemortem

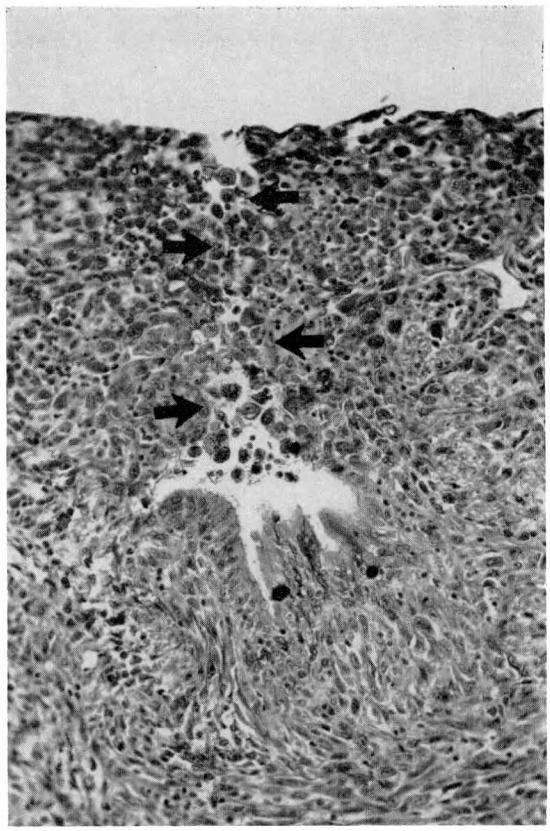


FIG. 1. Case 3. Metastatic osteogenic sarcoma tumor nodule in the periphery of the left lung (×250). The normal parenchyma is almost entirely replaced by masses of neoplastic cells. A fistula (arrows) extends from a bronchiole through friable tumor to the surface of the lung. (Air entered the pleural cavity via a ruptured subpleural bleb.)

bronchopleural communication and thus explain the genesis of pneumothorax. However, dense fibrous adhesions had made removal of the lungs difficult in most of these patients, and often the neoplastic tissue was very fragile and easily traumatized (Fig. 2). It is possible that the changes were artefactual and had been created at the autopsy table. In fact, rents and fissures in necrotic tumor nodules are seen not uncommonly in patients who never developed pneumothorax during life. It is therefore extremely difficult to positively establish the existence of an antemortem bronchopleural fistula, despite careful postmortem examination.

Lodmell and Capps[8] found interstitial air and subpleural blebs in 2 of their patients. They believe that tumor nodules act as ball valves to produce partial bronchiolar obstruction and hyperinflation of alveoli, thus initiating the mechanism described by Macklin,[9] who attributes the development of interstitial emphysema to the overdistention and break-down of alveolar "non-partitional bases" with subsequent dissection of air along perivascular routes to the surface. Should the resulting subpleural blebs rupture, a pneumothorax results. Pulmonary interstitial emphysema leading to subpleural bullae was not identified before or after death in any child in this series. However, the autopsy findings

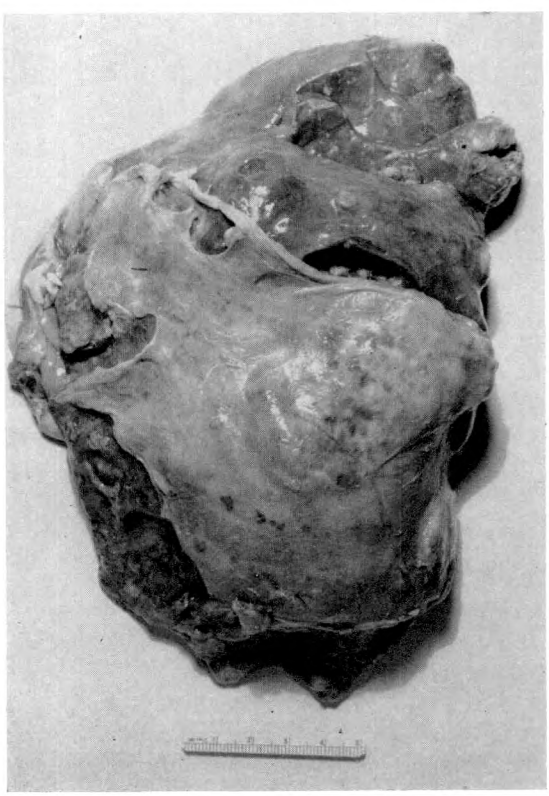


FIG. 2. Case 6. Anterior surface of the left lung (postmortem specimen). Dense adhesions obliterated much of the pleural cavity, and the lung was torn from its bed in removal. As a consequence, the rough and irregularly thickened pleural surface is disrupted in several areas. The trauma of removal also accounts for the deep fissure visible in the nodule with a denuded surface seen in the right upper corner of the figure. Many other metastases can be identified above the pleural level.

in another child were suggestive. Multiple 3–4 mm. blebs of air were found over the anterior aspect of the mediastinum of this boy who had an osteogenic sarcoma and pulmonary metastases but who never developed pneumothorax.

The evidence derived from the 13 children here reported suggests that the development of bronchopleural fistulae is the more frequent way by which air reaches the pleural cavity. The communications result from either direct extension through the pleura or after the formation of blebs which in turn rupture.

The clinical picture of spontaneous pneumothorax developing in association with pulmonary metastases shows many variations. Some of these are exemplified by reports of cases from the authors' series (Table 1) which follow.

REPORT OF CASES

Case 3. J.P. This male patient, with onset of disease at the age of fourteen, twisted his left knee while playing and developed a painful limp. A roentgenogram showed a lesion in the proximal left fibula and a biopsy was performed. The diagnosis was osteogenic sarcoma. He was then referred to The Children's Medical Center. Roentgen therapy was started, and 8,044 r were delivered to the left proximal tibia in 52 treatments over sixty-three days. Antitumor chemotherapy was also given during this interval. He remained well until four months after the onset of disease when pulmonary metastases were discovered on the right. Three weeks thereafter, roentgen therapy of the entire chest was started and 1,400 r were given in 10 treatments over fourteen days. After an initial diminution in size, the deposits became larger and more numerous. Six weeks following completion of therapy, a silent right pneumothorax with 30 to 40 per cent collapse of the underlying lung was identified roentgenographically. Spontaneous episodes of improvement occurred over the ensuing four weeks, although bouts of coughing became increasingly troublesome. No functional impairment was apparent despite roentgen evidence of persistent residual free air in the pleural cavity. Suddenly, severe coughing spells and pain in the left shoulder became manifest, and another roentgenogram revealed a tension pneumothorax on the left. There had been no definite prior roentgen evidence of left pulmonary involvement even as recently as nine days before. He was admitted to the hospital for observation and treatment. During the next three weeks, repeated left thoracenteses were performed with withdrawal of air, and tubes were inserted twice in an attempt to re-expand the lung. All these measures failed. In view of the persistent and uncontrollable bilateral pulmonary collapse, a left thoracotomy was done in order to identify and close the leaks. A subpleural emphysematous bleb measuring 3 cm. in diameter was found in the superior segment of the lower lobe. Air escaped through a round hole, about 0.5 cm. in diameter, at the apex of the bleb. No tumor was palpable in relation to this bulla, but microscopic examination revealed a bronchopleural fistula through a tiny 4 mm. metastasis (Fig. 1). Another ruptured bleb in relation to a metastasis, less than 2 cm. in diameter, was found along the pleural surface of the lingula near its juncture with the upper lobe. These lesions and a third subpleural nodule were removed. The surface of the lung was then scarified and dusted with talc, and the chest was closed around two tubes. The left lung reinflated promptly and remained expanded throughout the ensuing five months of life. The pneumothorax on the right followed a variable course, but at no time cleared completely. The patient continued to fail slowly and expired fifteen months after the first signs of disease.

Comment. The uncontrolled tension pneumothorax on the left, added to the right pneumothorax, severely restricted functional capacity. There was also an ever-present danger of complete bilateral collapse. Hospital care was considered essential under the circumstances. All conservative measures failed to secure re-expansion on the left and thoracotomy became necessary to achieve this end. There followed prompt improvement, enabling the child to leave the hospital and remain at home for the remainder of his life.

Case 5. R.M. This male patient, with onset of disease at the age of eleven, was well until he began to complain of pain in the right knee. One month later, swelling of the part had become noticeable and a biopsy of the right distal

femur was performed. The microscopic diagnosis was osteogenic sarcoma, and roentgen treatments were started, approximately 1,200 r depth dose being given in fifteen days. The child was then brought to The Children's Medical Center. Tumor chemotherapy was initiated, and roentgen therapy directed to the distal femur was continued, using 2 mev. technique.* An additional 6,000 r tumor dose was given, making a total of 7,200 r in fifty days. Six months later, roentgenograms showed a pulmonary deposit on the right, and four weeks thereafter, metastases were identified in the left distal femur. Eight months after the development of chest metastases and without prior symptoms referable to their presence, the patient suddenly became disoriented and perspired profusely. This was accompanied by moderate pain in the right chest. The entire episode lasted about twenty minutes. He was admitted to the hospital the next day when a chest roentgenogram showed a massive right-sided tension pneumothorax. The lung slowly re-expanded over the next seven weeks. Chemotherapy with various agents had been continued throughout his course, but the chest metastases and those in the left femur continued to enlarge. The right pneumothorax recurred two weeks after it had been resorbed, and on this occasion a thoracentesis was done with removal of the free air. His status continued to deteriorate rapidly and he died eighteen months after the onset of disease.

CASE 7. L.F. This female patient, with onset of disease at the age of nine, was in good health until she suddenly complained of pain in the left thigh and inability to stand. Two weeks thereafter a mass along the left iliac crest was noted. Roentgenograms showed an extensive osteolytic lesion involving most of the wing of the left ilium. No metastases in the lungs or elsewhere were present at that time. Radiation therapy of the ilium was started, and after a depth dose of 824 r in seven days, a biopsy was performed. The pathologic report was osteogenic sarcoma. The patient was then continued on 2 mev. radiation therapy.* She received an additional 2,290 r (depth dose) in sixteen days and one month later 3,900 r (depth dose) in twenty-nine days. Tumor chemotherapy was then initiated. She remained entirely well with no pulmonary symptoms until two months later, when she developed vomiting and slight pain anteriorly over the chest, which was aggravated by deep inspiration and coughing. Roentgenograms taken within the next few days demonstrated a tension pneumothorax on the right with complete collapse of the lung (Fig. 3*A*). The margins of the right lung showed numerous small metastatic nodules. These were also present on the left side. On the same day, a thoracentesis was performed on the right side and 600 cc. of air was removed. Two days thereafter, however, a tension pneumothorax and complete collapse of the lung were again demonstrated on the same side. Nine days later there supervened nausea, vomiting, and greatly increased respiratory embarrassment. Roentgenograms showed a tension pneumothorax and complete collapse of the lung still present on the right side. A pneumothorax also was present on the left with about 50 per cent collapse. (Fig. 3*B*). Bilateral thoracotomies for constant drainage of both pleural cavities resulted in considerable improvement. The tubes were removed when re-expansion was complete. Ten days later, pneumothorax recurred bilaterally, with more than 50 per cent collapse of the lungs on each side. The tubes were reinserted but only slight improvement resulted. She died one month later of severe pulmonary insufficiency, six months after the onset of disease.

At autopsy, hydropneumothorax was found on both sides. Each lung was collapsed and extensively involved with tumor masses. The visceral pleura appeared to be irregular and disrupted bilaterally due to necrotic tumor nodules and fibrous adhesions to the thoracic cage. Many of the pulmonary metastases in each lung showed necrotic centers.

CASE 8. S.B. This female patient, with onset of disease at the age of ten, developed painless swelling of the left calf which, on roentgen examination, was found to be caused by a tumor in the fibula. This was biopsied and the microscopic diagnosis of Ewing's tumor was made. Roentgen therapy was delivered to the entire left fibula over a thirty day period. The depth dose was calculated to be 6,400 r minimum and 7,100 r maximum. Meanwhile tumor chemotherapy was started. A mid-thigh amputation was then performed. Four months thereafter, pulmonary metastases on the left were visible on roentgenograms. These were treated with

* Cases 5 and 7 were treated through the kind cooperation of Dr. Joseph Marks and associates of the New England Deaconess Hospital.

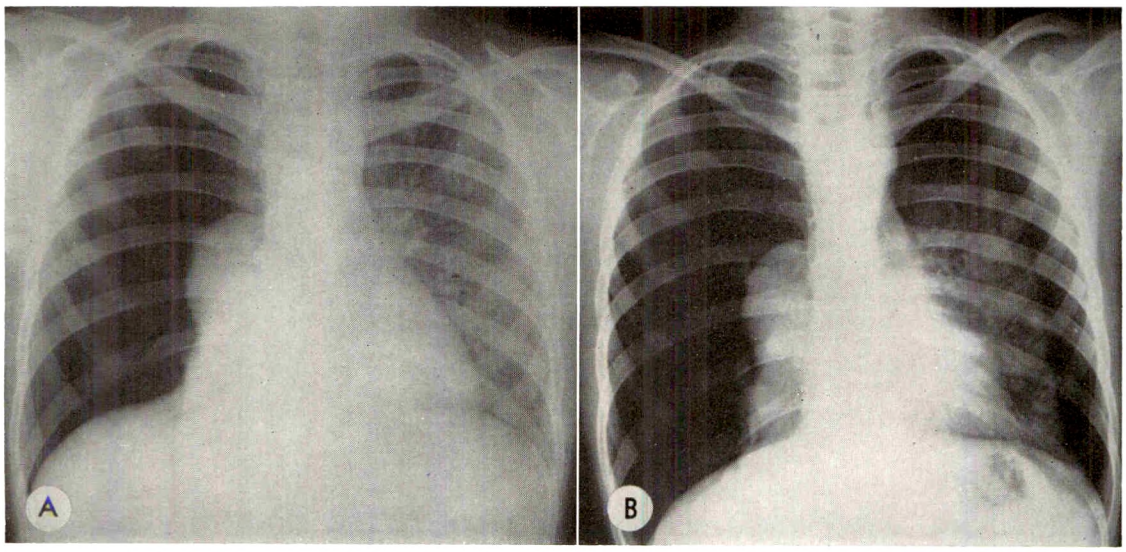


Fig. 3. Case 7. (*A*) Osteogenic sarcoma with bilateral pulmonary metastases. A spontaneous tension pneumothorax on the right is associated with complete collapse of the lung. This complication was the first indication that pulmonary deposits were present. (*B*) Ten days later. Pleural free air on the right persists despite attempts to secure permanent re-expansion. A spontaneous pneumothorax is now present on the left where multiple subpleural metastases are visible.

palliative irradiation with consequent temporary disappearance. Four months later, new lesions were visible on the right. Slow growth ensued over the next seven months, when exertional dyspnea and severe cough developed. A chest roentgenogram revealed the presence of a small, spontaneous tension pneumothorax on the right (Fig. 4). There were no further signs or symptoms attributable to the free air which resorbed during the following four weeks and never recurred. Her course continued to be downhill. The child expired thirty-three months after the onset of illness.

At autopsy, the entire thoracic cage was filled with tumor masses and fibrous adhesions largely obliterated the pleural cavities. Virtually no normal lung tissue could be identified grossly. Many of the neoplastic lesions showed extensive central necrosis.

Case 10. M.N. This female patient, with onset of disease at the age of six years, had been well until a palpable mass in the abdomen on the left was discovered. Excretory urography confirmed the presence of a left renal tumor, and a left nephrectomy was performed. The diagnosis on microscopic examination was Wilms' tumor. No pulmonary metastases were present at this time. Postoperative roentgen therapy of the left renal bed was given through opposing anterior and posterior portals. The depth dose was 3,500 r delivered in 22 treatments in twenty-seven days. Seven months later, a Horner's syndrome developed on the left and metastatic involvement was found in the left cervical lymph nodes. Pulmonary metastases on the right were also discovered at that time. Chemotherapy was started, and the roentgen therapy was directed to the cervical mass and to the pulmonary lesions, but her subsequent course was progressively downhill. Ten months after the nephrectomy, pleural fluid accumulated on the right, requiring thoracentesis for relief of respiratory distress. Two months thereafter, an asymptomatic spontaneous pneumothorax developed on the left. Gradual re-expansion of the lung took place during the remaining four weeks of life. She expired thirteen months after the onset of disease.

At autopsy, there were extensive metastases to the lungs, pleura, and tracheobronchial lymph nodes as well as to various extrathoracic sites. Bilateral hemothorax was also present, with severe compression atelectasis of the right lung.

Case 13. M.C. This female patient, with onset of disease at the age of eleven years, was first admitted to the hospital because of pain and swelling of the right thigh. An incomplete

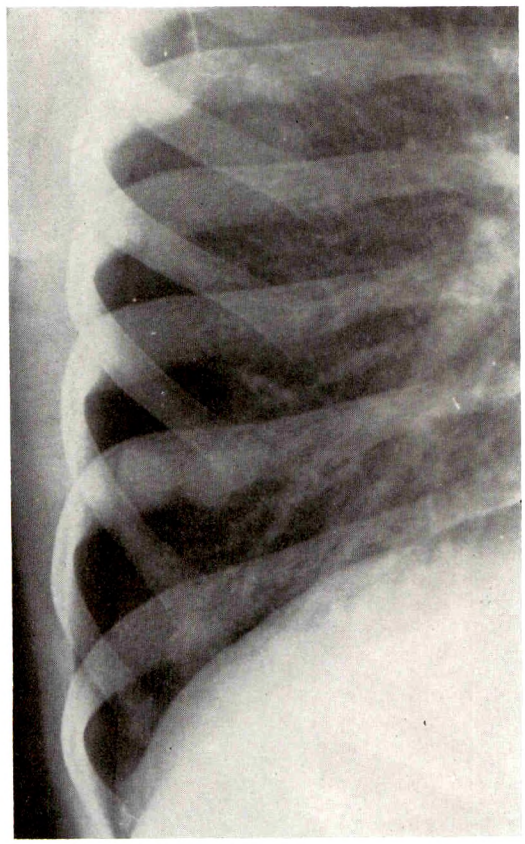


FIG. 4. Case 8. Ewing's tumor with pulmonary metastases and spontaneous pneumothorax. A peripheral tumor nodule bulges into the pleural cavity.

excision was performed with histologic diagnosis of hemangioendotheliosarcoma. Roentgen therapy was delivered to the right thigh. Pulmonary metastases became evident five months thereafter. Her condition deteriorated slowly despite the administration of multiple chemotherapeutic agents with and without roentgen therapy.

Fifteen months later there was a sudden episode of difficulty in breathing and chest pain which persisted over the ensuing four days. Roentgen examination of the chest showed a large tension pneumothorax on the right with complete collapse of the lung. A drainage tube was inserted into the right chest. Within twenty-four hours there was almost complete re-expansion of the lung. Further episodes of collapse occurred, but the lung completely re-expanded within two weeks. She continued to fail and died twenty-two months after her first symptoms.

At autopsy, there was extensive bilateral pulmonary disease, but no explanation for the genesis of the pneumothorax on the right was established.

DISCUSSION

There appears to be a disproportionate number of children with osseous tumors in whom spontaneous pneumothorax is a complication of pulmonary metastases. Chest roentgenograms demonstrating this combination suggest that the primary tumor originates in bone and most probably is an osteogenic sarcoma. A corollary is that patients with this neoplasm and lung deposits not infrequently develop a spontaneous pneumothorax. Of 19 children with osteogenic sarcoma metastatic to the lung, 4 manifested spontaneous pleural free air at some time during the course of the disease.

The complication can develop relatively early in the course of a child with a malignant process and pulmonary deposits. In some patients, the presence of free air in the pleural cavity is the first sign of lung involvement, previous roentgenograms having failed to demonstrate metastases. The pneumothorax may be silent and unsuspected clinically, only to be discovered as an incidental finding on roentgen examination. No treatment may be necessary under circumstances such as these, particularly since spontaneous re-expansion can occur. While the improvement may be only temporary in some patients, in others there is no recurrence.

The onset of pneumothorax is dramatic at times, and the patient develops the classic signs and symptoms of sudden chest pain, dyspnea and collapse. Prompt recognition and effective management of the complication, when disabling, can result in several more months of comfortable existence for the patient. Conservative measures may suffice, but vigorous treatment often becomes necessary. This may prove difficult, and thoracotomy sometimes is required before permanent re-expansion of the affected lung is obtained.

It has been suggested[8] that cough may be

a precipitating factor in the production of pneumothorax in these patients. Free air can develop, however, without any previous complaint referable to the chest. In Case 7, the onset of tension pneumothorax was the first indication of pulmonary metastases, the child having been free of symptoms with normal roentgenographic findings prior to that time.

No obvious association could be found between any form of chemotherapy and the development of this complication, nor was there any constant relationship to the use of roentgen therapy to the chest.

The roentgen differential diagnosis of spontaneous pneumothorax seldom presents any difficulty in these patients. Occasionally, extensive necrosis within huge pulmonary metastases with tracheobronchial communication can lead to confusion in diagnosis. The resultant air-fluid level may seem to reach the thoracic wall and simulate the appearance of a pneumothorax (Fig. 5). Metastases with associated large subpleural blebs have been described. An adult reported by Lodmell and Capps[8] was found at autopsy to have bullae as large as 20 cm. in diameter. Roentgenographically, these might simulate a localized pneumothorax. A child with metastatic osteogenic sarcoma (not included in this series) presented such a problem in roentgen diagnosis. It was not possible to state with certainty whether there was a small loculated pneumothorax or whether the appearance was caused by a collection of blebs beneath the pleura (Fig. 6)

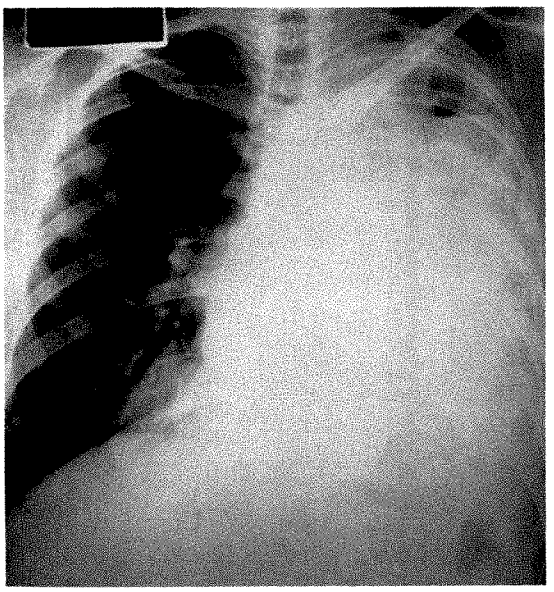


FIG. 5. Osteogenic sarcoma with pulmonary metastases. An air-fluid level is present in the left upper lung field and simulates a hydropneumothorax. At autopsy, no free air was present in the pleural cavity. There was extensive necrosis and liquefaction within an enormous tumor mass which virtually replaced the lung, but a thin shell of intact tissue remained peripherally.

SUMMARY

Spontaneous pneumothorax occurs infrequently in association with pulmonary metastases. Thirteen children with various malignant tumors who developed this complication are reported. Nine of these patients had bone tumors, as did 7 of the 8 children heretofore recorded. The apparent association of this secondary manifestation and malignant tumors primary in bone is discussed as are the probable routes by which free air reaches the pleural cavity.

The onset of pneumothorax may be asymptomatic in some instances but disabling in others. Since the complication may occur early in the course of the disease, prompt detection and treatment can secure for some patients relative comfort during the remaining months of life.

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We are indebted to Drs. Sidney Farber and William T. Green for making available the clinical data of these patients.

ADDENDUM

Since this paper was prepared for publication, an additional case has come to our attention. Dargeon, in his book "Tumors of Childhood" (Paul B. Hoeber, Inc., New York, 1960), reports the case of a nine year old boy with an angiosarcoma,

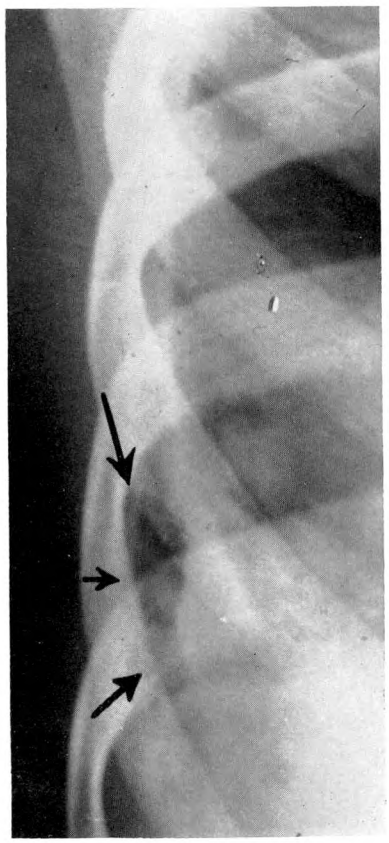


FIG. 6. Osteogenic sarcoma with pulmonary metastases. A small collection of air is visible immediately beneath the parietal pleura (arrows). The appearance could be produced by a small loculated pneumothorax or by subpleural blebs. At autopsy, two weeks after this roentgenogram was made, extensive adhesions were found in the area, but neither free air nor bullae were identified.

primary in the sacrum, with bilateral pulmonary metastases and bilateral pneumothorax.

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VOL. 86, NO. 6

BLEEDING ESOPHAGEAL VARICES IN THE PRESENCE OF A NORMAL SPLENOPORTOGRAM

A CASE REPORT

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PERCUTANEOUS splenoportography was originally devised to provide anatomic and functional information on the portal venous system to the surgeon planning a shunting procedure. A clinical diagnosis of portal hypertension, supported by routine laboratory and roentgenographic studies, has usually been made beforehand. Recently, refinements in technique, particularly in rapid serial roentgenography, have led to a more widespread use of this examination. At present, splenoportography is no longer restricted to candidates for surgical shunting but is now also advocated by many as a diagnostic procedure in upper gastrointestinal bleeding. In this regard, surprisingly meager data are available in the literature concerning the diagnostic accuracy of splenoportography. In general, however, all investigators have verified the high degree of accuracy that might be anticipated theoretically. Thus, Turner, Sherlock and Steiner[1] consider venography the method of choice in demonstrating esophageal varices and state: "If portal venography fails to show a gastroesophageal collateral circulation, bleeding from varices is most unlikely." Bergstrand and Ekman[1] reported filling of collaterals in all patients with portal hypertension and expressed the opinion that barium swallow studies never demonstrated varices that did not visualize at venography. Rousselot *et al.*[9] state: "We expected and found in the portogram, coronary-gastroesophageal collaterals in *all* cases."

We have recently been distressed by our failure to demonstrate collaterals in a patient with portal hypertension and obvious varices. For this reason, the following case is presented together with some discussion concerning the possible hemodynamic mechanisms involved.

REPORT OF A CASE

This sixty-seven year old white retired railroad worker was referred to the Hospital of St. Raphael because of weakness and hematemesis. The admission diagnosis was bleeding peptic ulcer. Six days before admission, the patient noted tarry stools and vague epigastric discomfort not relieved by meals. He was seen by his private physician and placed on an ulcer regimen of antacids and antispasmodics. One day prior to, and on the day of, admission, he vomited considerable amounts of bright red and coffee ground material.

Six months previously, he had noted black stools over a one week period, associated with weakness and mild epigastric discomfort. On an ulcer regimen, the symptoms subsided and no further studies were done. There was a long history of chronic alcoholism but no previous episodes of jaundice. Traumatic amputation of his left lower leg had resulted from a railroad accident ten years before.

Physical examination revealed an extremely pale but alert and oriented male. No jaundice or spider angiomata were noted. The lungs and heart were normal. A questionable nontender liver edge was felt but the spleen was not palpable. The blood pressure was 130/70 and the pulse 120.

The hemoglobin on admission was 4 gm. and the hematocrit 17 per cent. The bromsulphalein was 20 per cent, but the remaining liver function studies, including total protein, A/G ratio, bilirubin, prothrombin time, cephalin flocculation, thymol turbidity, cholesterol, alkaline phosphatase, and blood ammonia, were normal.

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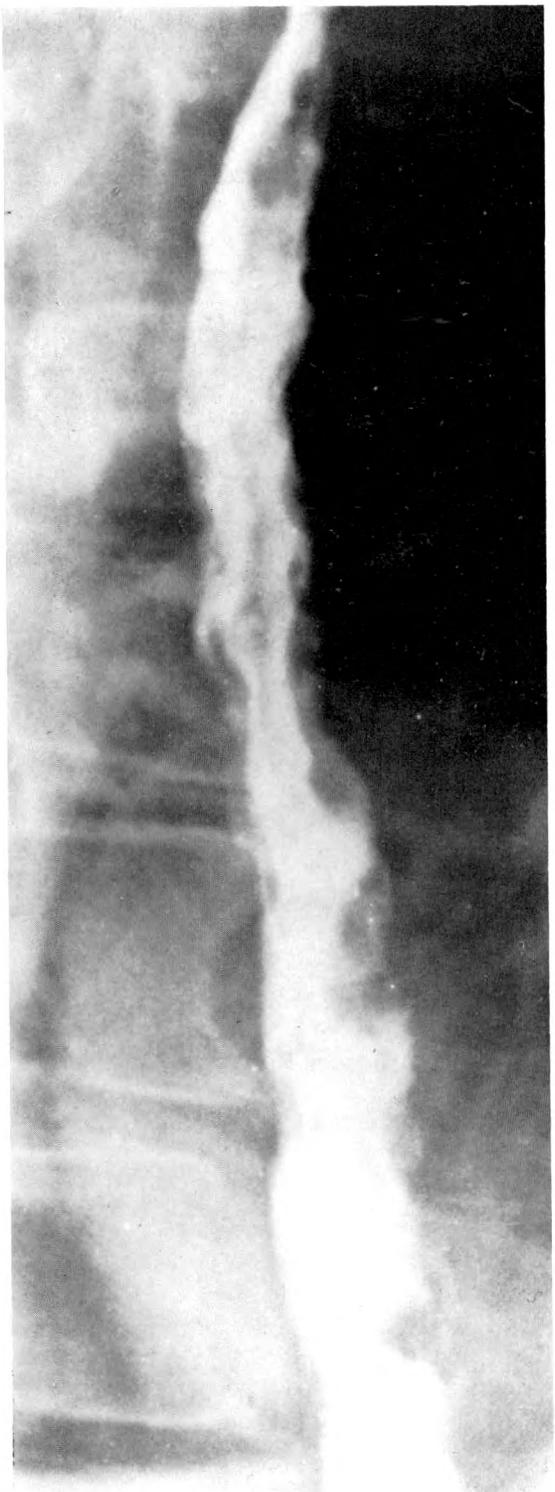


FIG. 1. Barium swallow study demonstrating large varices extending the length of the esophagus.

An upper gastrointestinal series revealed large varices of the distal esophagus and probable gastric varices (Fig. 1).

During the first three hospital days, multiple transfusions raised the hemoglobin to 11.5 gm. and all evidence of active bleeding subsided. In view of the well compensated hepatocellular function, a splenoportal shunt was contemplated. In preparation for this procedure, percutaneous splenoportography was performed. Although not palpably enlarged, the spleen was easily punctured and the intrasplenic pressure (corrected to the anterior body of the first lumbar vertebra[8]) averaged 410 mm. H_2O. Following the manometric determination, 50 cc. of 90 per cent hypaque was injected manually over a period of six to eight seconds. Roentgenograms at the rate of two per second were obtained commencing with the beginning of the injection and extending over a fourteen second period. At no time was any collateral circulation or retrograde filling of the portal tributaries demonstrated. Patent splenic and portal veins were visualized. The intrahepatic portal branches were sparse and tortuous, with the typical "tree in winter"[10] appearance associated with cirrhosis (Fig. 2).

Failure to demonstrate any roentgenographic signs of portal hypertension (*i.e.*, retrograde filling of portal tributaries, visualization of collateral circulation, dilated splenic and portal veins with delayed transit) in the presence of

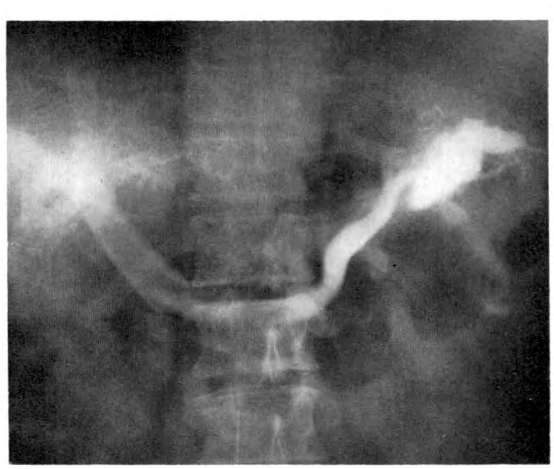


FIG. 2. The initial splenoportogram without evidence of collateral filling. Note the filling defect at the entrance of the superior mesenteric vein. Intrasplenic pressure at this time was 410 mm. H_2O.

marked intrasplenic hypertension and obvious esophageal varices raised some doubt concerning the correctness of the clinical diagnosis. A localized left coronary vein occlusion can produce varices and a normal splenoportogram, but such a patient would not benefit by portal vein decompression. Carcinoma of the gastric cardia frequently extends submucosally up the esophagus and occasionally may simulate varices.

Consequently, four days after the first splenoportogram, esophagoscopy was performed. Very large varices were encountered 7 cm. below the cricopharyngeus and extended the length of the esophagus. The following day, a second percutaneous splenoportogram was performed, technically similar to the first examination in all details. On this occasion, retrograde filling of the inferior mesenteric vein and visualization of short gastric veins draining into large esophageal varices confirmed the original diagnosis of cirrhosis with portal hypertension and varices (Fig. 3). The corrected intrasplenic pressure on this occasion was 370 mm. H_2O.

An end-to-side portacaval anastomosis was performed (Dr. Philip Wade) resulting in a pressure drop of 110 mm. H_2O (300→190) when the shunt was opened. A repeat barium swallow study during convalescence showed almost complete disappearance of the varices, a few widened longitudinal folds remaining in the distal esophagus.[4]

The patient was admitted five months following surgery in a stuporous condition with a blood ammonia of 105. He responded rapidly to low protein feedings, his sensorium clearing in thirty-six hours and the blood ammonia dropping to 42. Unfortunately, no barium swallow examination was done at this time. However, there has been no recurrence of gastrointestinal bleeding.

DISCUSSION

Most reviews of splenoportography have stressed its accuracy in demonstrating portal collateral circulation, particularly the cardioesophageal collateral system. We believe that serial roentgenograms are required for an adequate examination and that failure to visualize known varices on a single roentgenogram at the conclusion of

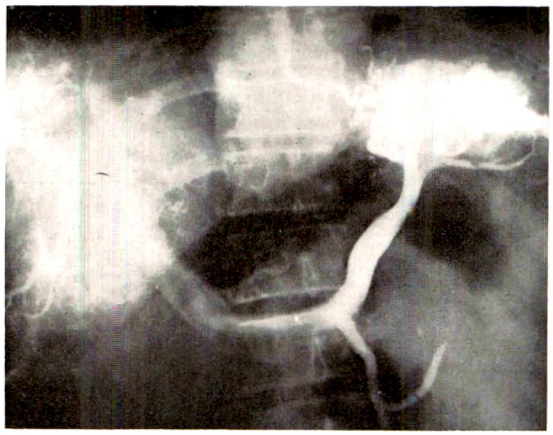


FIG. 3. Note the retrograde filling of the inferior mesenteric vein and the dilated short gastric veins filling tortuous esophageal varices. Intrasplenic pressure was 370 mm. H_2O.

injection does not exclude their filling at an earlier or later phase. Bruwer and Hallenbeck[3] include in their material a single case (Case 5) in which splenoportography showed no evidence of collaterals in spite of a portal pressure of 520 mm. H_2O and varices previously demonstrated on barium swallow study. However, only a single roentgenogram was taken and the authors themselves admit that "more than one roentgenogram is required for satisfactory demonstration of the functional hemodynamic status of the portal system." Figley *et al.*[6] mention 3 cases with proved varices which did not fill but they also incriminate inadequate roentgenography. In addition, no mention is made of intrasplenic pressure measurements or the visualization of other collateral systems.

The time sequence of examinations may have an important bearing on collateral filling. It is conceivable that varices, demonstrated on barium swallow examination during acute hepatic decompensation, might fail to fill during splenoportography at a later date. Intensive medical therapy may undoubtedly ameliorate acute hepatic congestion with a resultant increase in transhepatic portal blood flow and a drop in portal pressure. Previously overburdened

TABLE I

Examination	Hospital Day	Collaterals Demonstrated	Portal Pressure
1st gastrointestinal study	2	+	
2nd gastrointestinal study	7	+	
1st splenoportogram	8	−	410 mm. H_2O
esophagoscopy	14	+	
2nd splenoportogram	16	+	370 mm. H_2O

collateral networks may then cease to function or diminish markedly in size. However, this possibility fails to explain the findings in our case (Table 1) in which collateral filling occurred only after clinical improvement and a drop in portal pressure.

The natural history of esophageal varices has been well demonstrated by Palmer,[7] who performed serial esophagoscopies on 133 patients with proved cirrhosis and varices, noting a marked day to day variation in their size and extent. In 35 of the subjects, varices were not seen during at least one esophagoscopic examination. In addition, he found little correlation between varix size and the clinical course of the patient or the level of portal pressure. He explained this variation by pointing out that esophageal varices constitute but one of several portosystemic shunting systems and that different outflow tracts may function at different times. Theoretically, splenoportography should demonstrate all collateral networks functioning at the time of the examination and should, therefore, be more reliable than either a barium swallow study or esophagoscopy where only the submucosal component of the cardioesophageal shunt can be seen. Failure to fill varices at splenoportography, provided other shunt systems are demonstrated, does not exclude their presence. However, failure to demonstrate any collaterals at all in the presence of portal hypertension, as happened in our case, would seem to exclude a large functioning collateral network. Certainly, there must be a stage early in the development of cirrhosis when elevated portal pressure alone suffices to perfuse the liver and no collaterals are present. This was the stage of disease with which we thought we were dealing. If uncertain or equivocal varices had been demonstrated on barium swallow examination, we would have pursued it no further.

From our personal experience and a review of the literature, a small but definite group of patients with portal hypertension and functioning portosystemic shunts seem to have a normal splenoportogram. Steiner *et al.*[11] from a large experience, report 2 patients with varices not demonstrable on splenoportography, but they make no mention of other collaterals. Evans[5] reports 4 cases showing extensive varices on barium swallow studies with apparently normal portograms. However, 2 of these patients had normal intrasplenic pressures and the third, an unsatisfactory pressure tracing. It is conceivable that, with normal portal pressures, none of the shunts was functioning at the time of the examination. (He does not mention the time relationships between barium swallow examination and splenoportography). This leaves but one case similar in all respects to our own, *viz.*, a normal splenoportogram in the presence of portal hypertension and proved collaterals.

It is difficult to conceive of a mechanism to explain this phenomenon. Evans[5] suggests that breath holding during the examination might elevate the pressure in the caval and azygos systems with temporary arrest or even reversal of the flow through collaterals. It is our policy to have the patient breathe shallowly throughout the examination except when the needle is inserted or withdrawn. A prolonged injection time resulting in an inadequate bolus of contrast material should produce faint opacification of all vascular channels, not merely failure of collateral filling. Moreover, Bergstrand and Ekman[2] have shown in dogs that variations in the rate of intrasplenic injection, provided adequate visu-

alization is obtained, produce no variation in the presence or absence of collateral filling. It is possible that streaming phenomena within the portal vein could sweep the entire bolus of contrast material directly to the liver in spite of the presence of multiple functioning shunts.

No adequate hemodynamic explanation may be offered for the above case. Nevertheless, it does caution against complete reliance upon splenoportography for the diagnosis of esophageal varices. Although splenoportography is the most reliable single technique available at present, it is not infallible since it can yield normal findings in the presence of bleeding varices.

SUMMARY

A case of bleeding esophageal varices is presented with two percutaneous splenoportographic studies. The first examination was normal but the second study, performed under similar conditions, revealed the varices. Possible hemodynamic mechanisms are considered.

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INTRAVENOUS ABDOMINAL AORTOGRAPHY IN THE DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF ANEURYSMS OF THE SPLENIC, HEPATIC AND RENAL ARTERIES*

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THERE is general agreement that the definitive diagnosis of aneurysm of the splenic, hepatic or renal artery is established by contrast visualization. The era of abdominal aortography was ushered in by dos Santos *et al.*[7] in 1929 when they described their lumbar aortography. At first, largely because of the alarming vascular damage and fatalities in the animals studied by Henline and Moore[30] and reported from this center, there was reluctance to perform translumbar aortography. Later, it became quite popular,[8,32,33,47,54,55] but had been virtually abandoned by many as a diagnostic procedure when fatalities and increasing complications were reported.[5,25,28] However, it is still highly regarded in many centers for diagnosis of renal arterial malformations and for discovery of the cause of renal hypertension, and with proper care and precaution can be accomplished with minimum risk.[5,10,35,36] Lately, percutaneous retrograde aortography and selective arteriography have been widely used, probably because of improvements in catheters,[42,48] spring guides, contrast agents, and mechanical injectors.[9]

A recent account of an intravenous method of abdominal aortography, employing a modification of the Robb-Steinberg technique, by bilateral, simultaneous and rapid injection of concentrated organic iodides and precisely timed roentgenography documents the capability of the procedure to readily opacify aneurysms of the aortic arch, abdominal aorta and its branches.[48] Because very little special or expensive apparatus is required, it can easily be performed in the average well-equipped radiology department. Abdominal aortography and peripheral arteriography, thereby, become practical and generally available diagnostic techniques.

In this report, intravenous abdominal aortography for diagnosis of aneurysms of the splenic, hepatic and renal arteries is illustrated, discussed and compared with arterial puncture. In this way, the place of intravenous abdominal aortography in establishing or excluding disease of the abdominal aorta and its branches can be assessed and evaluated.

FINDINGS

ARTERIOSCLEROTIC SPLENIC ARTERY ANEURYSM

Three patients with arteriosclerotic aneurysms of the splenic artery have been examined since we began using intravenous abdominal aortography in 1959. The first case, (Fig. 1, *A* and *B*) recently reported,[49] was studied after a roentgenogram of the hips, made because of backache, had disclosed calcifications in the left upper quadrant (Fig. 1*A*). An intravenous abdominal aortogram showed that the larger of the two calcifications was a splenic artery aneurysm, the other a calcified lymph node (Fig. 1*B*).

Another patient[50] (Fig. 2, *A–D*), a woman aged sixty-seven, with gastrointestinal complaints, was found to have an eggshell type of calcification just medial to the lesser curvature of the stomach (Fig. 2*A*). Intravenous abdominal aortograms demonstrated a splenic artery aneurysm (Fig. 2, *B* and *C*). Figure 2*D* is a view of the aneurysm at operation, while Figure 2*E* is the excised specimen.

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The third case, that of a sixty-five year old woman (Fig. 3, *A–D*), was unusual because the presenting complaint was hematuria, which subsequently was found to be due to hemorrhagic cystitis. The conventional roentgenograms showed a 2.5 cm. round calcified mass in the left upper quadrant, seemingly related to the left kidney (Fig. 3, *A* and *B*). Intravenous abdominal aortograms, however, clearly differentiated it from the kidney substance and enabled the establishment of the diagnosis of an arteriosclerotic splenic artery aneurysm (Fig. 3, *C* and *D*). Figure 3*E* shows the splenic artery aneurysm *in situ* at the time of operation. The aneurysm and spleen were removed; the convalescence was uncomplicated.

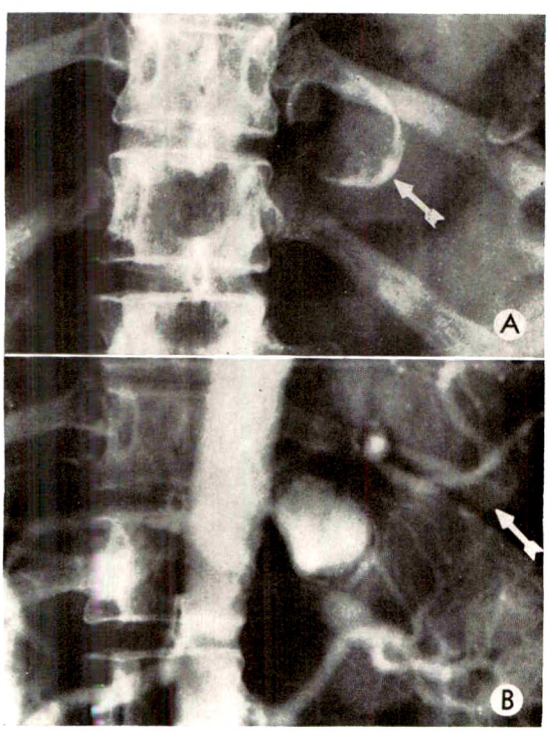


Fig. 1. *Arteriosclerotic aneurysm of the splenic artery in an asymptomatic fifty-four year old housewife.* (*A*) Enlarged (close-up) conventional roentgenogram showing two calcific shadows in the left upper quadrant. The larger lesion is egg-shell in type and located between the eleventh and twelfth ribs adjacent to the eleventh and twelfth vertebrae. The smaller rectangular lesion is in an interspace above. (*B*) Enlarged (close-up) intravenous abdominal aortogram showing the opacified splenic artery aneurysm. Note that the upper calcific shadow (arrow) is not opacified.

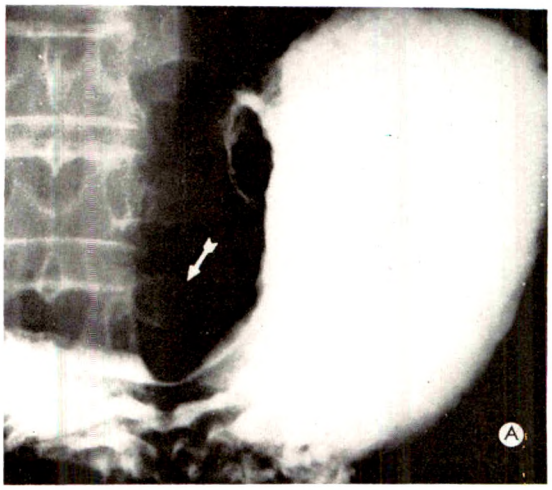


Fig. 2. *Arteriosclerotic splenic artery aneurysm in a sixty-seven year old woman with vague left upper quadrant flatulence and discomfort.* (*A*) Enlarged (close-up) roentgenogram of the barium filled stomach showing a rounded 1.5 cm. egg-shelled type of calcification adjacent to the left border of the spine just below the eleventh left rib (arrow).

HEPATIC ARTERY ANEURYSM

The case of an arteriosclerotic aneurysm of the hepatic artery in a seventy-two year old man (Fig. 4, *A–C*) was also recently reported.[50] The aneurysm, encountered during an exploratory operation for subacute cholecystitis and cholelithiasis, was not removed. Four years later, when we began employing abdominal aortography, the hepatic artery aneurysm was visualized. Figure 4*A* is the conventional roentgenogram of the abdomen showing a small calcification in the right upper quadrant. An intravenous abdominal aortogram showed an aneurysm of the hepatic artery (Fig. 4, *B* and *C*).

RENAL ARTERY ANEURYSM

Two patients with renal artery aneurysms have had intravenous abdominal aortography. The first, a fifty-five year old woman (Fig. 5, *A–C*) had hypertension (190/110 mm. Hg), peripheral vascular disease, and a characteristic signet-ring calcific shadow in the pelvis of the right kid-

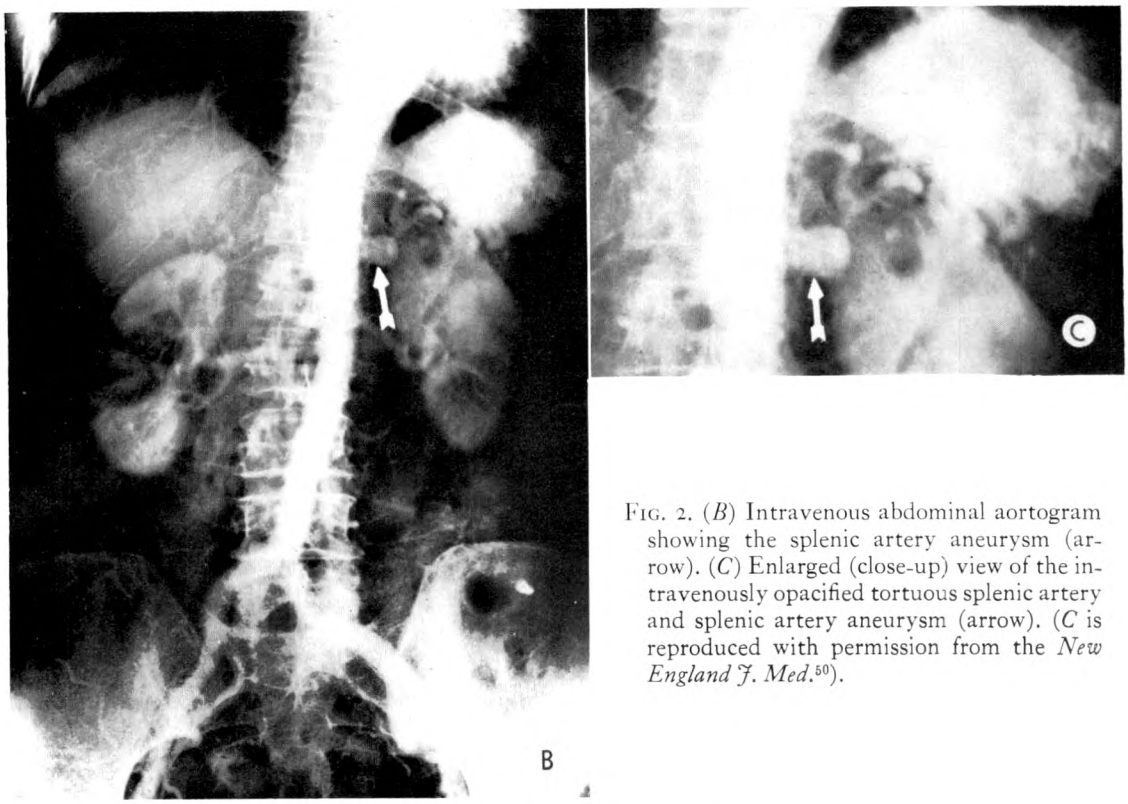


FIG. 2. (*B*) Intravenous abdominal aortogram showing the splenic artery aneurysm (arrow). (*C*) Enlarged (close-up) view of the intravenously opacified tortuous splenic artery and splenic artery aneurysm (arrow). (*C* is reproduced with permission from the *New England J. Med.*[50]).

ney (Fig. 5, *A* and *B*). An intravenous abdominal aortogram demonstrated a hypoplastic left renal artery and kidney, and arteriosclerotic endarteritis of the abdominal aorta and iliofemoral arterial tree (Fig. 5*C*). The left renal artery was poorly visualized, probably because of arteriosclerotic endarteritic involvement of the vessel. The right renal artery was not abnormal; an aneurysm in the hilus of the

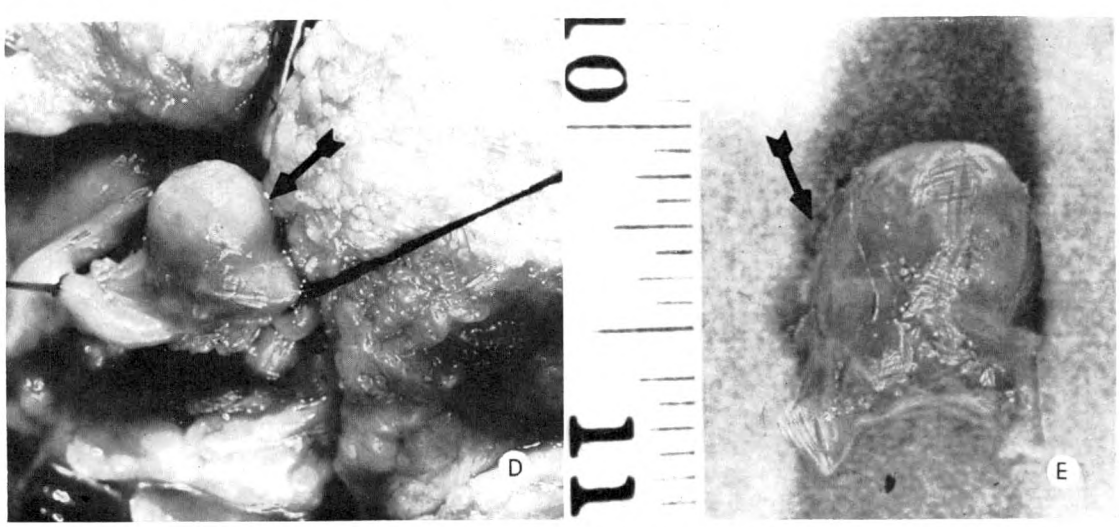


FIG. 2. (*D*) Photograph of the splenic artery aneurysm (arrow) at operation. (*E*) The excised splenic artery aneurysm.

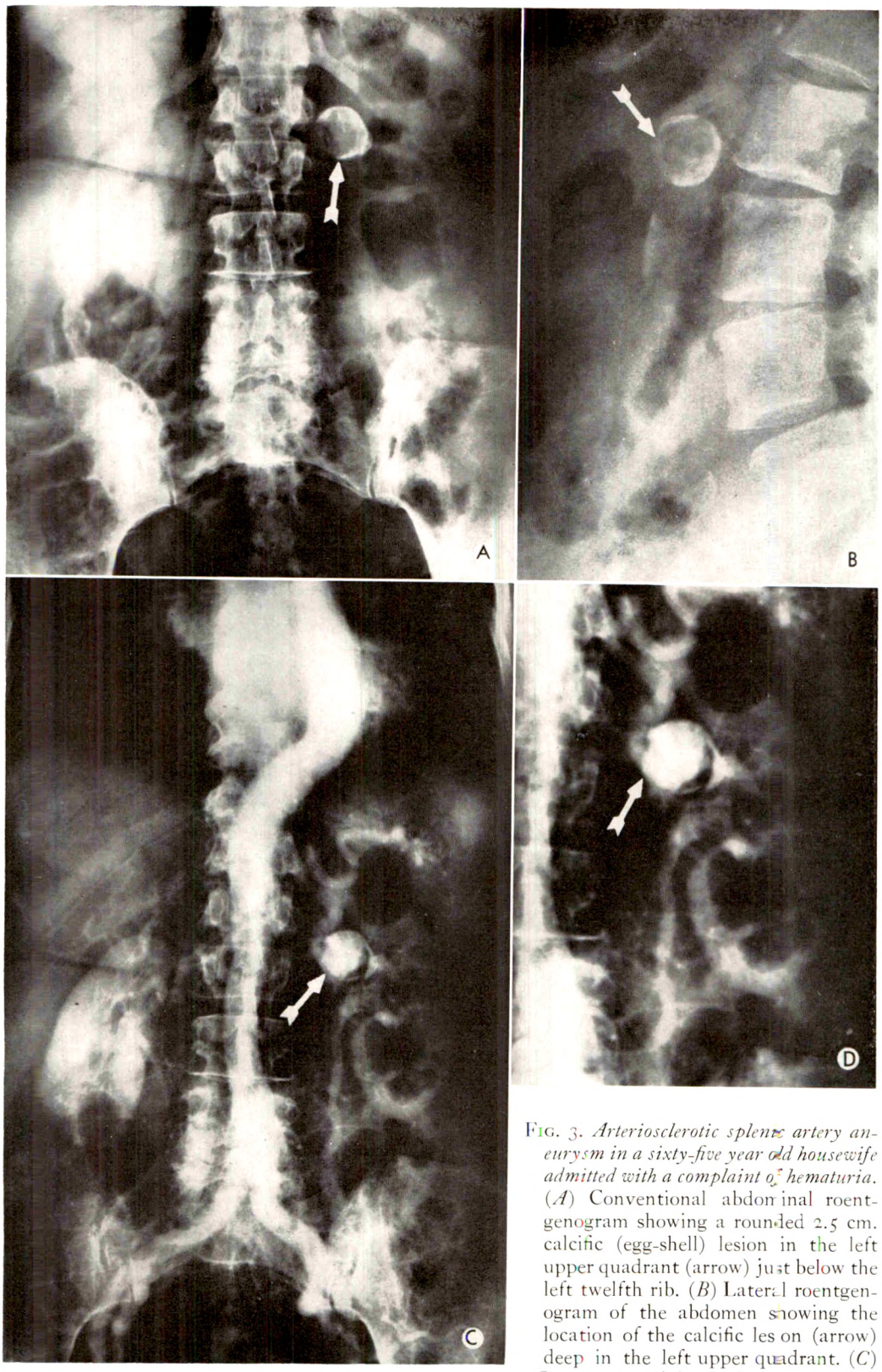


FIG. 3. *Arteriosclerotic splenic artery aneurysm in a sixty-five year old housewife admitted with a complaint of hematuria.* (*A*) Conventional abdominal roentgenogram showing a rounded 2.5 cm. calcific (egg-shell) lesion in the left upper quadrant (arrow) just below the left twelfth rib. (*B*) Lateral roentgenogram of the abdomen showing the location of the calcific lesion (arrow) deep in the left upper quadrant. (*C*) Intravenous abdominal aortogram disclosing the splenic artery aneurysm (arrow) and the tortuous splenic artery. Tortuosity of the abdominal aorta and common iliac arteries is seen. (*D*) Enlarged (close-up) view of the opacified tortuous splenic artery and splenic artery aneurysm (arrow). Note the relation to the aneurysm, close to, but separate from, the hilus of the kidney.

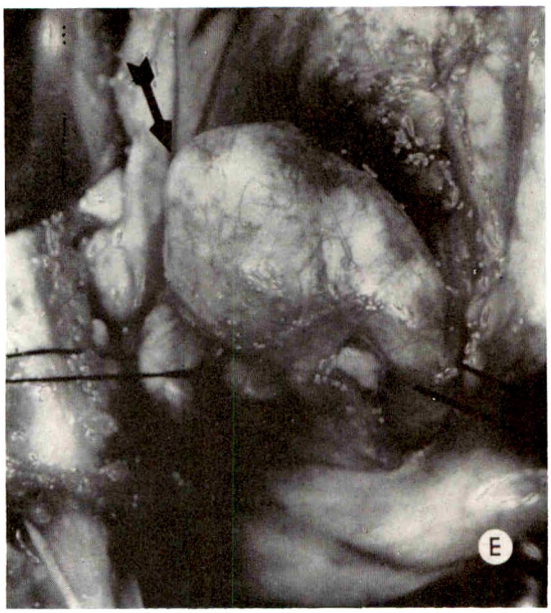
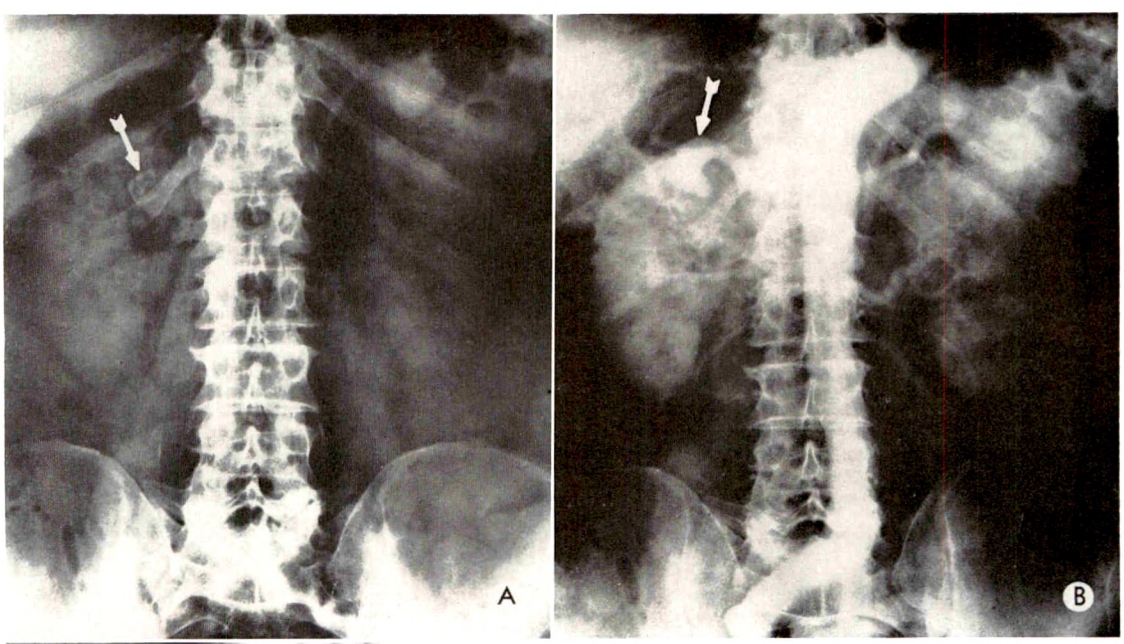


FIG. 3. (*E*) Photograph of the splenic artery aneurysm at the time of operation.

right kidney was not demonstrated (Fig. 5*C*). However, because of the characteristic pyelographic findings (Fig. 5, *A* and *B*), an exploratory operation of the right kidney was performed and disclosed a clotted calcific 1 cm. aneurysm of the right renal artery as it entered the hilus (Fig. 5*D*). Because preoperative studies had revealed decreased function in the left kidney and the left renal artery and kidney were hypoplastic, right nephrectomy was not done. A year following operation, the hypertension was still unrelieved and the patient was unimproved.

The second patient was a forty-eight



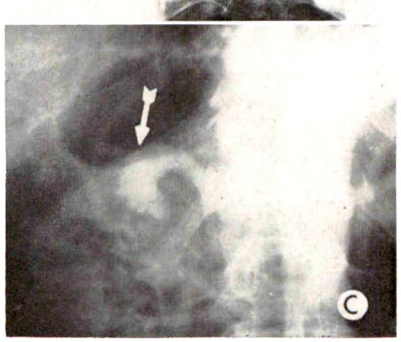


FIG. 4. *Arteriosclerotic hepatic aneurysm in a seventy-two year old man, visualized four years after its discovery at operation.* (*A*) Conventional frontal roentgenogram of the abdomen showing a rounded 1.5 cm. in diameter calcific area (arrow) between the eleventh and twelfth right ribs close to the border of the spine. (*B*) Intravenous abdominal aortogram showing tortuosity of the abdominal aorta and common iliac arteries. The hepatic artery is dilated at its origin, it then becomes aneurysmal in the calcific region (arrow). (*C*) Enlargement of the involved area showing the aneurysm (arrow). (*C* is reproduced with permission from *The New England J. Med.*[50])

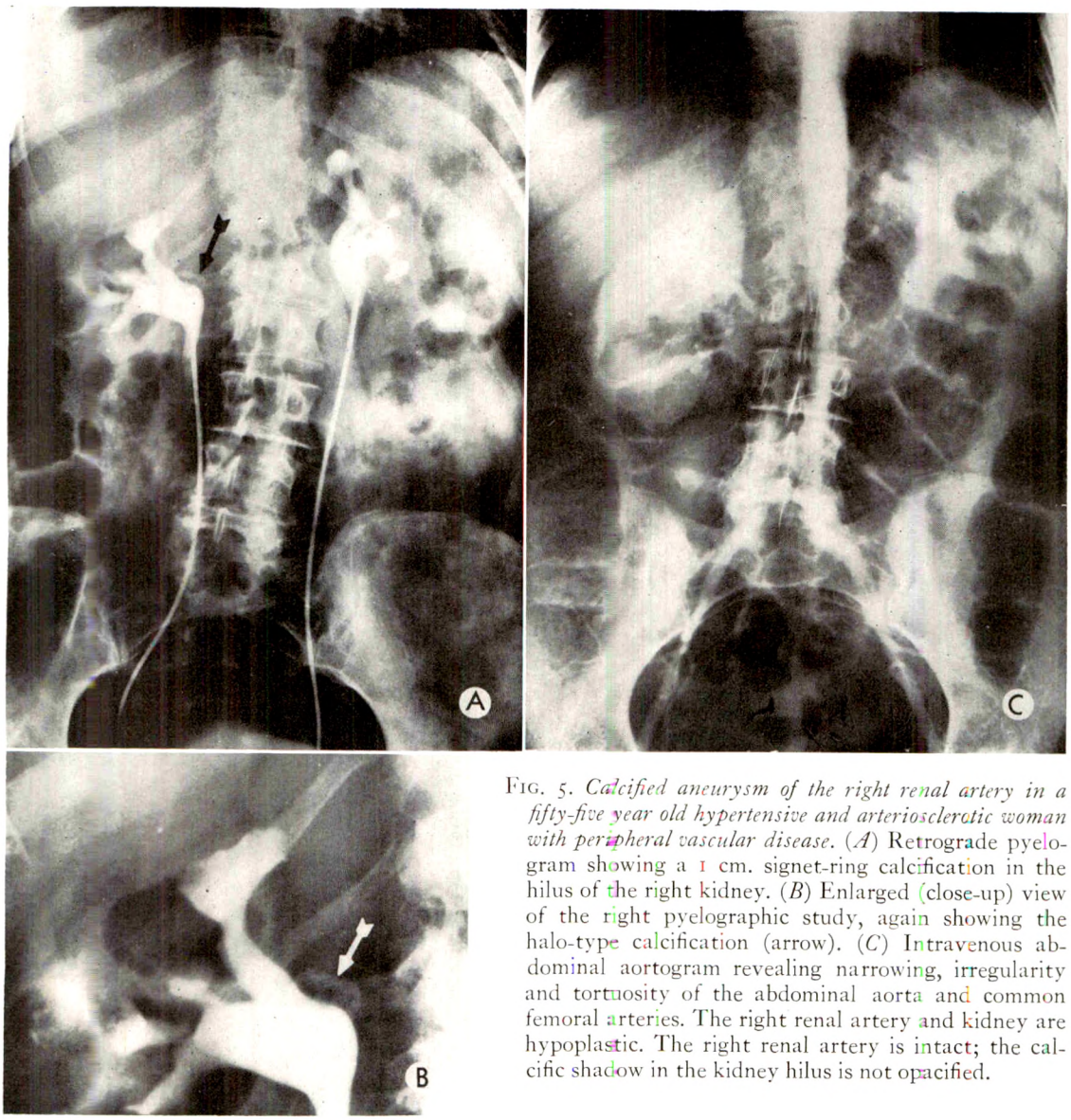


Fig. 5. *Calcified aneurysm of the right renal artery in a fifty-five year old hypertensive and arteriosclerotic woman with peripheral vascular disease.* (*A*) Retrograde pyelogram showing a 1 cm. signet-ring calcification in the hilus of the right kidney. (*B*) Enlarged (close-up) view of the right pyelographic study, again showing the halo-type calcification (arrow). (*C*) Intravenous abdominal aortogram revealing narrowing, irregularity and tortuosity of the abdominal aorta and common femoral arteries. The right renal artery and kidney are hypoplastic. The right renal artery is intact; the calcific shadow in the kidney hilus is not opacified.

year old man (Fig. 6, *A–C*), who also had hypertension (170/115 mm. Hg). Deformity of the right renal pelvis was demonstrated on a retrograde pyelogram (Fig. 6*A*). The intravenous abdominal aortogram revealed a 1 cm. aneurysm of the right renal artery (Fig. 6, *B* and *C*). This finding was confirmed at operation, but in this instance, because previous studies had demonstrated good left kidney function, a right nephrectomy was performed and the patient became normotensive.

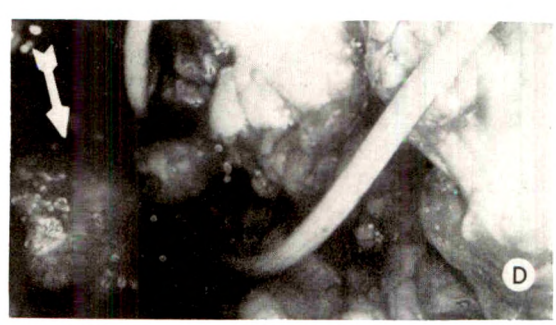


Fig. 5.(*D*) Photograph at operation revealing the clotted calcified aneurysm (arrow).

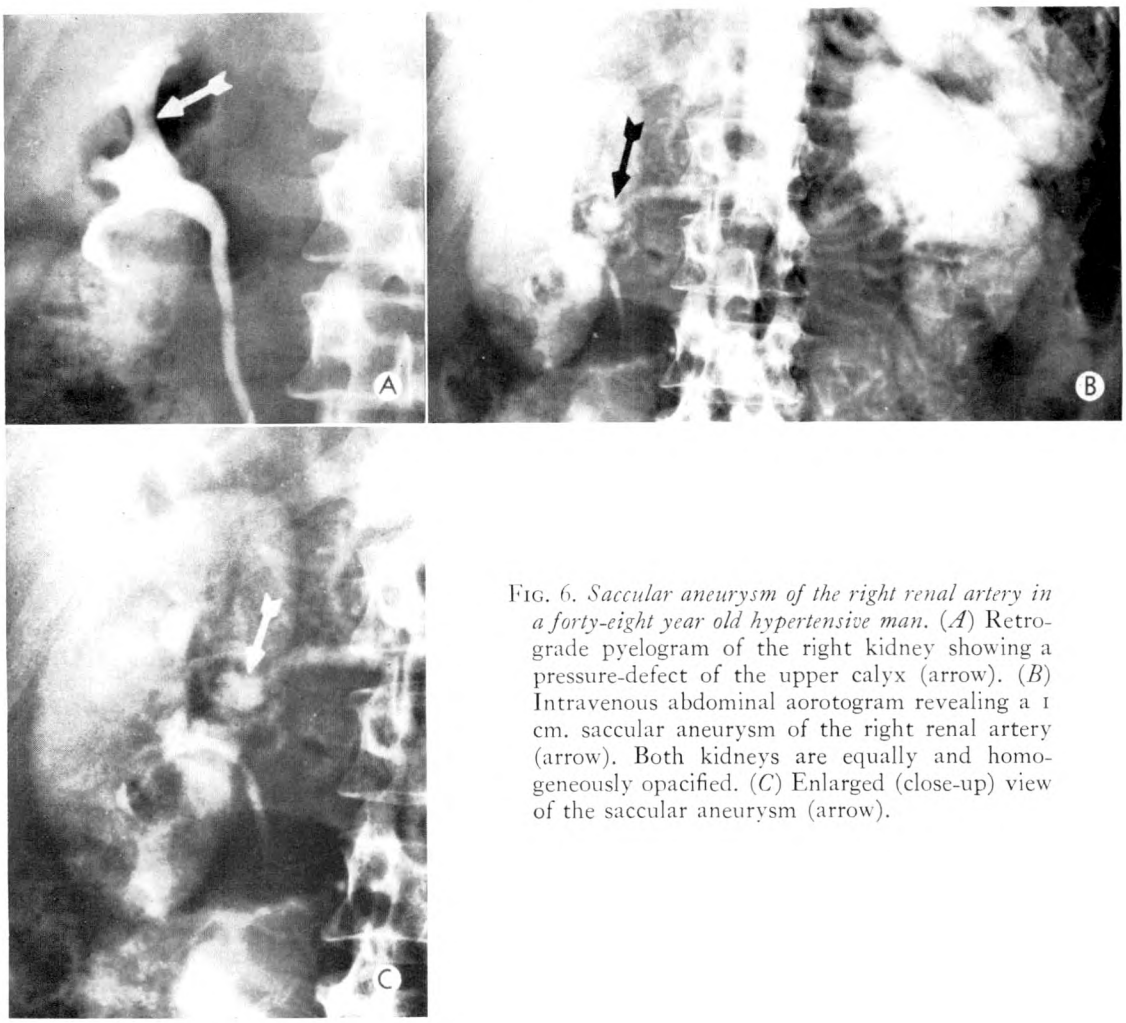


FIG. 6. *Saccular aneurysm of the right renal artery in a forty-eight year old hypertensive man.* (*A*) Retrograde pyelogram of the right kidney showing a pressure-defect of the upper calyx (arrow). (*B*) Intravenous abdominal aorotogram revealing a 1 cm. saccular aneurysm of the right renal artery (arrow). Both kidneys are equally and homogeneously opacified. (*C*) Enlarged (close-up) view of the saccular aneurysm (arrow).

DISCUSSION

Owens and Coffey,[37] in a thorough review of splenic artery aneurysms, discussed the incidence, pathogenesis, pathologic and clinical features and the tendency of these aneurysms to rupture during pregnancy. More recently, Culver and Pirson,[6] and Sheps and his co-workers[44] have reviewed the subject. There appears to be general agreement among surgeons that, once the diagnosis of splenic artery aneurysm is suspected, surgical exploration and excision of the aneurysm is essential to prevent rupture. Indeed, following the pioneer paper of Lindboe,[27] who emphasized that rounded, egg-shell calcific shadows in the left upper quadrant were likely to be aneurysms of the splenic artery, routine exploration of the abdomen and excision of the aneurysm and spleen have been advocated. Von Ronnen,[53] however, believes that only if the calcified splenic aneurysm is large, causes symptoms, or enlarges is surgery indicated.

Diagnosis of splenic artery aneurysms is dependent mainly upon roentgenography. In 15 per cent of the cases reviewed by Owens and Coffey,[37] there were valuable diagnostic roentgen clues consisting of either a pulsatile mass in the posterior wall of the stomach or round or oval-shaped thin lined (egg-shell) calcifications located in the upper left quadrant of the abdomen (Fig. 1, *A* and *B*; 2*A*; and 3, *A* and *B*).

Differentiation between gastrointestinal and renal calcifications can readily be made by contrast roentgen studies. Pancreatic stones are more difficult to differentiate,[53] but now that a method for opacifying the aorta via the intravenous route exists, the definitive diagnosis need not be delayed.

Owens and Coffey[37] also emphasize that awareness of the possible existence of a splenic artery aneurysm is very important in establishing the diagnosis. Among the clinical findings cited by these authors are pain in the left upper quadrant, flatulence and splenomegaly. These are so nonspecific that they provide little aid in diagnosis. Other signs of greater significance, although rare, are a palpable and occasionally pulsatile tumor in the left hypochondrium. However, the "egg-shell" opacities in the left upper quadrant, unrelated to the renal or gastrointestinal systems, provide the most significant clues of splenic artery aneurysms.

Of interest, is the case showing opacification of the splenic artery aneurysm (Fig. 1*B*) and not of the adjacent calcification. At operation the latter turned out to be a calcified lymph node. Multiple aneurysms of the splenic artery have been reported in the literature, but these have been round, lined by calcific walls and have contained mottled densities, in marked contrast to the irregularly shaped and often homogeneously calcified structure of the calcified lymph node (Fig. 1*A*).

Hepatic artery aneurysms are rare. Browning, Clauss and MacFee[2] in a recent report of 2 cases stated that they found 121 cases in the medical literature. Their 2 cases, 2 other cases reported since then,[17,24] the case of a child,[23] and the one case reported above bring the total to date to only 127. Notable reviews of the subject[12,16,20,40,45,46,51] indicate that males with hepatic artery aneurysms predominate at a ratio of 3 to 1. The average age is thirty-eight years. There also appears to be general agreement that the most common causes of hepatic artery aneurysms are infection (60 per cent), arteriosclerosis (22 per cent), and trauma (10 per cent).[30] The aneurysms may be intrahepatic or extrahepatic, the latter being more common and varying from a small size (a true aneurysm) to a huge (false type) hematoma. Both tend to be adherent to surrounding tissues by firm fibrous adhesions that compress the surrounding structures, especially the bile ducts. The majority of hepatic artery aneurysms are solitary; only in 11 instances were multiple aneurysms found. The hepatic artery itself rather than the branches is usually involved.

Hepatic artery aneurysms, like all aneurysms, have a tendency to rupture. The peritoneal cavity is a favorite site, and sudden shock and death due to hemorrhage are common. Direct perforation into the duodenum and stomach has also been reported.[9,15,52] Perforation may also occur into the biliary duct system and cause hematemesis or melena, or both.[31] As a result, a triad of symptoms referable to hepatic artery aneurysms has become recognized. These are right hypochondriac pain, gastrointestinal hemorrhage, and jaundice due to pressure on biliary ducts. However, these too, are so nonspecific that they are of little value in the differential diagnosis. A pulsating right upper quadrant mass with a systolic bruit and enlargement of the liver are more valuable but rarer findings. About 36 cases of hepatic aneurysm have been diagnosed during life,[2,24,26] all, as in our case at exploratory laparotomy. Accordingly, a high index of suspicion coupled with a contrast visualization study of the abdominal arterial tree promises to be the most effective way of making the diagnosis.

In our case (Fig. 4*A*), a right upper quadrant calcification accurately localized the site of the arteriosclerotic hepatic aneurysm. The American[22] and French[21] literature contains references to this sign. However, since calcification usually occurs only in the arteriosclerotic hepatic artery aneurysms and since these comprise only about one quarter of all aneurysms, it probably is an uncommon finding. Bruwer and

Hallenbeck,[4] after retrospective study of a case, suggested that a filling defect in the duodenum may also be of diagnostic significance. In our patient, however, probably because of the small size of the aneurysm, contrast duodenal studies were normal.

Recent accounts of survival following surgical correction of hepatic aneurysms indicate that a new era in treatment of this lesion has evolved.[2,11,13,18,24,26,38] Indeed, excision of the celiac axis for repair of an hepatic artery aneurysm has been reported.[18,24] Similarly, excision of an arteriosclerotic celiac artery aneurysm with anastomosis of the hepatic artery to the origin of the celiac axis was successfully performed by Schumacker and Siderys.[41] Accordingly, preoperative diagnosis is no longer of academic interest. In this connection, however, it must be mentioned that our patient with the arteriosclerotic aneurysm (Fig. 4, *A–C*) had been asymptomatic during the four year period following its discovery at laparotomy.

Although rare, aneurysms of the renal artery are being encountered more frequently. This is apparently due to the increasing use of aortography, especially in young hypertensives in order to determine if there is a renal vascular cause for the hypertension.[35,36] Harrow and Sloane[19] in 1959 reported 5 new cases, reviewed the literature and pointed out that because of the use of aortography over one-third of the total of 180 cases of renal artery aneurysms had been reported within the six year period from 1951 to 1957.

Ever since Renck's[39] classic description of the roentgen appearance of calcified renal artery aneurysms, a signet-ring, halo-shaped calcification just medial to the renal pelvis has become established as pathognomonic of the lesion (Fig. 5, *A* and *B*).[29,34,53] This sign constitutes strong evidence for renal artery aneurysms,[34] but only about 25 per cent of the cases of renal artery aneurysms show this calcification. Harrow and Sloane[19] recently found that 69 of the total 180 cases reported in the literature had been diagnosed because of the characteristic calcific ring shadow. Aortography, chiefly translumbar, established the diagnosis of 28 of the 180 cases.

In the absence of calcification, a renal artery aneurysm cannot be excluded and should be suspected when there is an unexplained deformity of a calyx (Fig. 6*A*). Contrast aortography of the abdominal aorta either by the intravenous, retrograde or translumbar routes is clearly indicated in such cases, especially because, in marked contrast to the calcified aneurysms of the renal artery, the noncalcified aneurysms have a tendency to rupture.[19] Accordingly, here too, a high incidence of suspicion that a renal artery aneurysm is the cause of an unknown hypertension, poor or nonfunctioning kidneys, unexplained extrarenal or intrarenal noncalcified space-occupying lesions is necessary.

DIFFERENTIAL DIAGNOSIS

In cooperative patients, intravenous abdominal aortography may be expected to provide a highly satisfactory contrast study of the abdominal aorta and its branches (Fig. 7, *A* and *B*). However, in a recent case of a twenty-six year old woman with hypertension, the tortuosity of the splenic artery prevented adequate visualization of the left renal artery (Fig. 8*A*). Accordingly, percutaneous transfemoral renal arteriography[17] was performed with the patient in a slightly oblique position, and stenosis of the proximal portion of the left renal artery with poststenotic dilatation of the distal segment of the left renal artery (Fig. 8*B*) was demonstrated. Splenectomy followed by anastomosis of the splenic artery to the poststenotic segment of the left renal artery resulted in the blood pressure returning to normal levels.

Tortuous linear calcifications of the splenic artery in the left upper quadrant due to arteriosclerosis are readily differentiated from aneurysms of the splenic artery (Fig. 9) by the regular pattern of the calcifications. An echinococcus cyst may appear exactly like a splenic artery

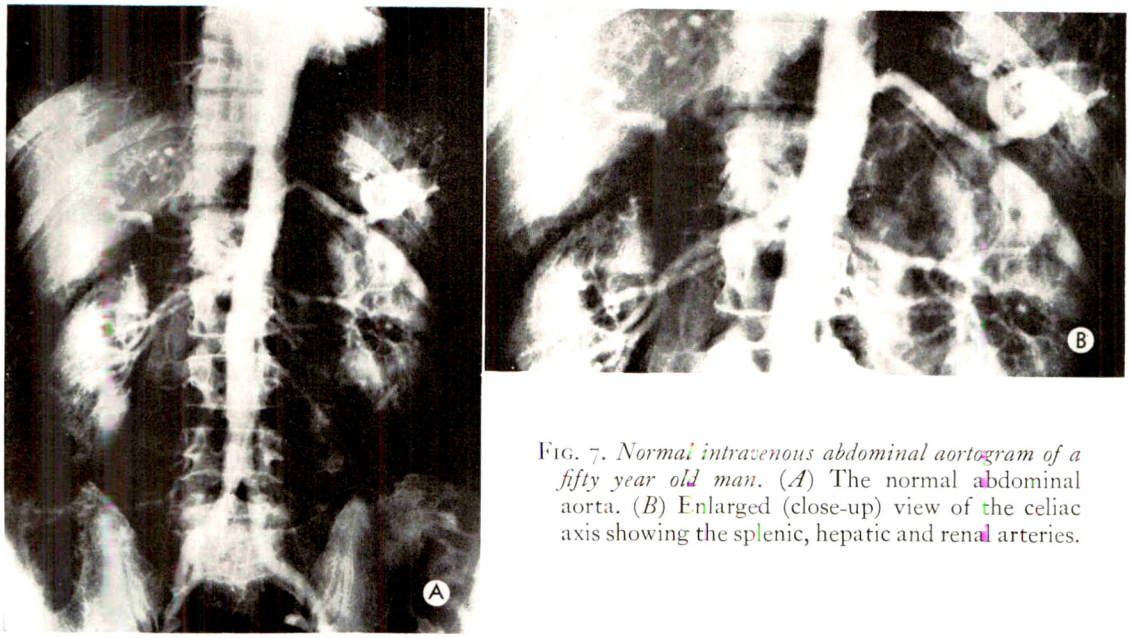


Fig. 7. *Normal intravenous abdominal aortogram of a fifty year old man.* (*A*) The normal abdominal aorta. (*B*) Enlarged (close-up) view of the celiac axis showing the splenic, hepatic and renal arteries.

aneurysm and be differentiated only when contrast materials fail to opacify it. In such an instance intravenous abdominal aortography (Fig. 10) by failing to opacify the egg-shell calcification excluded an aneurysm. Rarely, splenic artery aneurysms may be confused with renal artery aneurysms, especially if calcific shadows are in the vicinity of the left kidney and there are complaints referable to the urinary system.

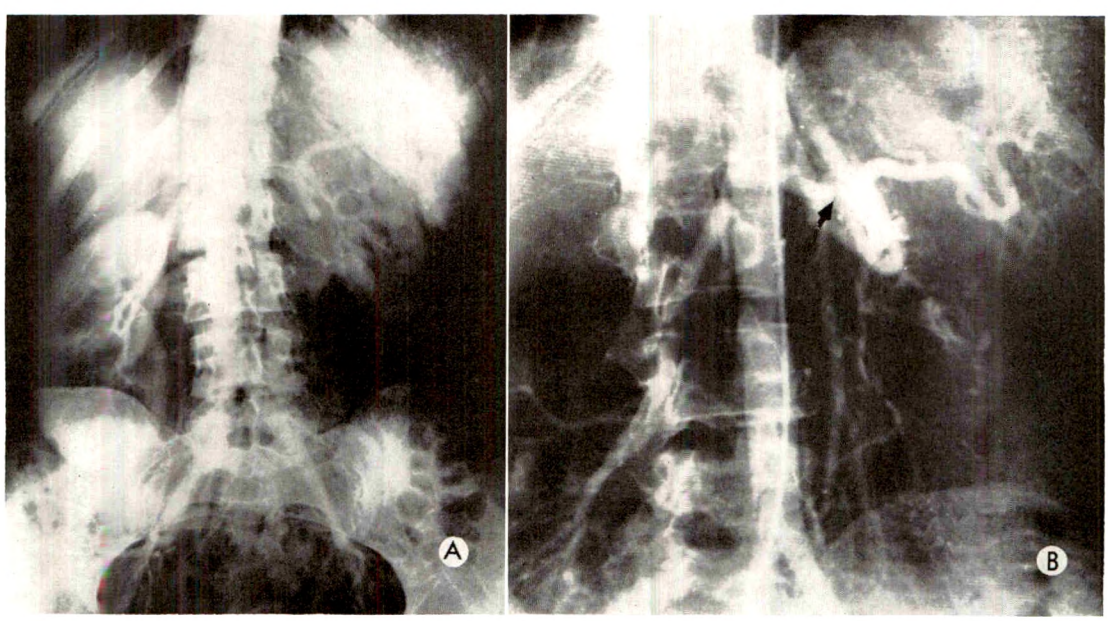


Fig. 8. *Hypertension due to left renal artery stenosis in a twenty-six year old woman.* (*A*) Intravenous abdominal aortogram showing tortuosity of the splenic artery obscuring the left renal artery (arrow). (*B*) Percutaneous translumbar renal arteriogram disclosing the site of stenosis of the left renal artery (arrow) with poststenotic dilatation of the distal portion of the renal artery.

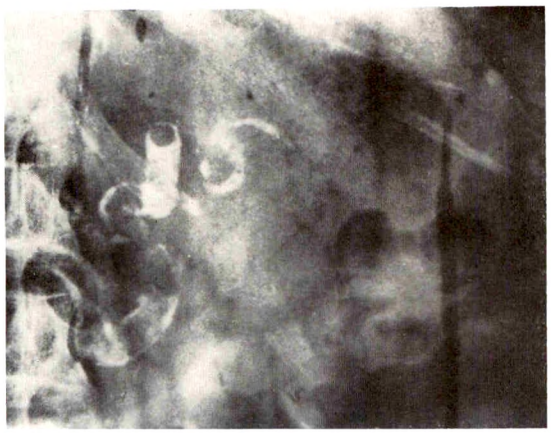


FIG. 9. *Calcification and tortuosity of the splenic artery in a ninety year old physician.* The regular, though dilated, caliber of the artery is characteristic of arteriosclerotic involvement of the splenic artery and should be differentiated from saccular aneurysms of the splenic artery.

Usually, the larger size of the calcified lesion in the left upper quadrant (Fig. 3*A*) is against it being due to a renal artery aneurysm. Here, too, intravenous aortography readily established the diagnosis of splenic artery aneurysm, and operation proved it.

Gallstones may be confused with hepatic and renal artery aneurysms. The characteristic appearance of a laminated gallstone (Fig. 11) should not be difficult to recognize. Intravenous abdominal aortography in this patient was performed because of hypertension.

Admittedly, intravenous abdominal aortography does not achieve the high degree of radiopacity produced by translumbar or retrograde aortography. However, the morbidity of the translumbar approach is probably greater than that of intravenous abdominal aortography in certain patients. For example, one patient (Fig. 12) was found to have a right renal artery aneurysm in the course of retrograde aortography, performed in order to locate the site of coarctation of the abdominal aorta. Demon-

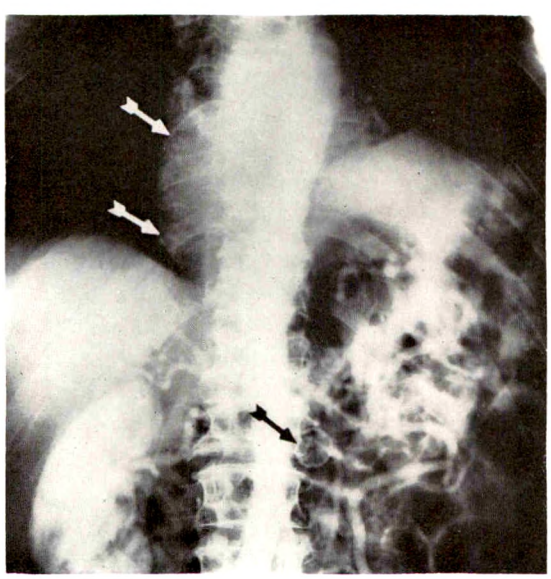


FIG. 10. *Egg-shell calcification in the left upper quadrant of the abdomen due to an echinococcus cyst (lower arrow) simulating a splenic artery aneurysm.* Note the opacified tortuous arteriosclerotic abdominal aorta. The splenic artery is also markedly tortuous, but the egg-shell calcification is not opacified. Note also (upper arrows) the mediastinal (nonopacified) calcification due to a huge mediastinal echinococcus cyst.

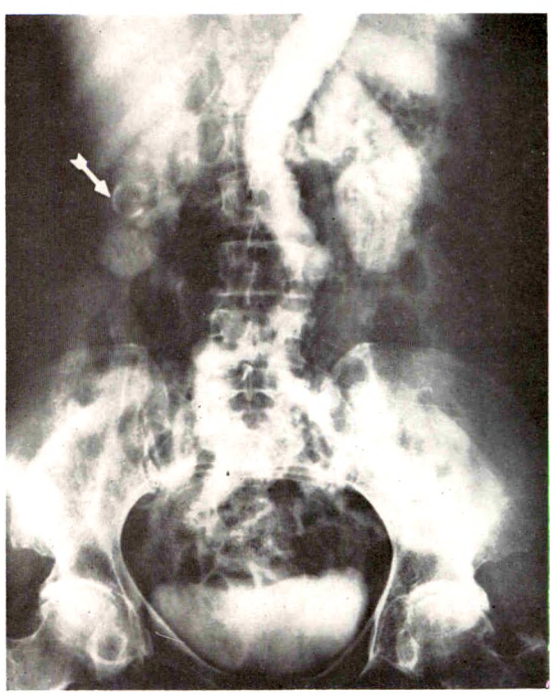


FIG. 11. *Intravenous abdominal aortogram revealing a tortuous abdominal aorta.* The left renal artery is hypoplastic and the left kidney is not opacified. A laminated gallstone in the right upper quadrant is easily differentiated from a right renal and/or hepatic artery aneurysm.

stration of the site of coarctation was successful, but a severe hypotensive reaction with renal shut-down following injection of diodrast was almost fatal.[14] Indeed, 2 fatalities in patients with coarctation of the abdominal aorta and renal artery stenosis after retrograde catheterization have recently been reported.[3] Accordingly, it would appear that intravenous abdominal aortography in such cases may be sufficient in establishing the diagnosis of coarctation of the abdominal aorta and renal artery stenosis without resorting to arterial catheterization.

SUMMARY AND CONCLUSIONS

A significant advance in the diagnosis and differential diagnosis of aneurysms of the splenic, hepatic and renal arteries has been achieved with intravenous abdominal aortography. This consists of rapid, simultaneous and bilateral injection of concentrated contrast organic iodides and precisely timed roentgenography. Inexpensive special needle-stopcock units, syringes and the use of apparatus ordinarily on hand for roentgen examination of the gastrointestinal or genitourinary systems make the procedure generally available and practical.

In a series of 350 consecutive patients who had had intravenous abdominal aortography, 3 were found to have arteriosclerotic aneurysms of the splenic artery; one had an arteriosclerotic hepatic artery aneurysm. Two hypertensive patients had renal artery aneurysms. All the cases of splenic artery aneurysm exhibited the classic roentgen features of arteriosclerotic artery aneurysms; namely, large, oval shaped, eggshell calcifications in the left upper quadrant. In one patient left upper quadrant calcifications were found during an incidental roentgen study of the abdomen. The second patient had vague epigastric discomfort. In the third, hematuria and the inability to dissociate the calcifications from the renal shadow made differential diagnosis more difficult. However, intravenous abdominal aortography was definitive. Excision of the splenic artery and the aneurysm, and splenectomy were curative in every case.

An arteriosclerotic hepatic artery aneurysm, found in one case during exploratory operation, was definitively diagnosed four years later by intravenous abdominal aortography. Excision of the aneurysm was not advised because of the asymptomatic state of the patient and because of advanced arteriosclerotic changes in the rest of the abdominal aorta.

A signet-ring calcification in the hilus of the right kidney in one case was strong evidence for the diagnosis of a renal artery aneurysm even though intravenous abdominal aortography failed to opacify the lesion. The diagnosis was confirmed at operation, but nephrectomy was not done because of severe abdominal aortic endarteritis with left renal artery and kidney disease. In this case, the relentless progress of the hypertension was not altered. In contrast, another patient with a saccular

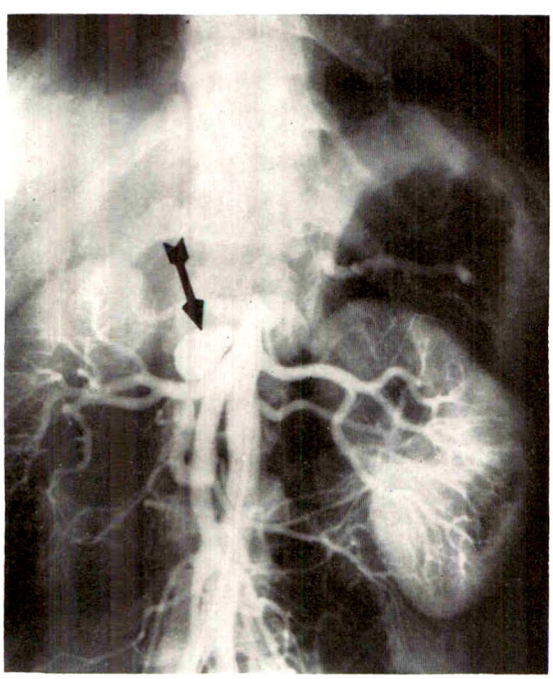


FIG. 12. *Retrograde abdominal aortogram revealing a saccular right renal artery aneurysm in a twelve year old girl with coarctation of the abdominal aorta.* (Reproduced with permission from *Surg., Gynec. & Obst.*[14].)

aneurysm of the right renal artery, revealed by intravenous abdominal aortography, had excellent kidney function and a normal renal arterial blood supply in the opposite kidney. Nephrectomy resulted in the patient becoming normotensive.

Intravenous abdominal aortography is also important in the differential diagnosis of aneurysms from other lesions of the abdominal aorta and its branches. Failure to opacify calcified or egg-shell lesions which mimic splenic or renal artery aneurysms is good evidence against the diagnosis of aneurysm. Occasionally, a thrombosed aneurysm will fail to opacify. However, its proximity and relationship to the opacified vessel will allow proper diagnosis. Gallbladder, intrahepatic and renal stones may often be readily identified on contrast studies of the gallbladder and genitourinary system; calcified echinococcus cysts, mesenteric lymph nodes and pancreatic stones may prove more difficult to differentiate from the calcifications of aneurysms. Failure to opacify such lesions by aortography, of course, excludes aneurysms. Although aortography may also fail to opacify calcified and thrombosed renal artery aneurysms, fortunately, in such instances, the characteristic signet-ring (halo) calcification, located in the hilus of the kidney, is of great significance.

Finally, intravenous abdominal arteriography cannot always be relied upon to exclude renal arterial stenosis. These cases may probably be better evaluated by percutaneous transfemoral renal arteriography or translumbar arteriography.

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The authors are grateful to Drs. S. W. Moore and Victor F. Marshall who respectively gave permission for publication of the operative photographs (Fig. 3*E* and 5*D*).

ADDENDUM

Since this paper was submitted for publication, J. A. Spittel, J. F. Fairbairn, O. W. Kincaid and W. H. ReMine have reviewed the experience in 15 cases of splenic artery aneurysm at the Mayo Clinic (*J.A.M.A.*, 1961, *175*, 452–456). They, too, stress the importance of aortography in diagnosis.

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EDEMA OF THE INTERURETERIC RIDGE—A USEFUL ROENTGEN SIGN*

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THE purpose of this paper is to call attention to edema of the interureteric ridge of the urinary bladder as a useful finding in roentgen diagnosis. The usual cause for the edema is a stone that has become impacted in the distal ureter or has recently passed through the ureteral orifice.

In 1948, Edling[1] reported his observations of the interureteric ridge. He described its normal appearance and the changes seen on 135 consecutive urograms of patients who had symptoms of ureteral calculi. He recorded the distinct bowed contour, continuous and cephalically concave, of the normal interureteric ridge. The distance between the ureteral contrast and the craniad contour normally was 2 to 3 mm., using a 15° caudocephalad projection of the roentgen-ray beam with the patient in the supine position.

In more than half of Edling's series the interureteric ridge was demonstrated. Swelling of the affected side of the interureteric ridge was present in 37 cases in which a uretero-vesical calculus was seen. In 4 cases without visible stones the swelling was attributed to a recently passed or non-opaque calculus.

In 1954, Filho[2] discussed this sign and noted that swelling of the interureteric ridge subsided within forty-eight hours after passage of the ureterovesical calculus.

We have studied 125 unselected consecutive intravenous pyelograms in an attempt to determine the incidence of visualization of the interureteric ridge, the frequency of edema and the value of this sign in the diagnosis of ureteral calculus. The duration of the edema after the stone passed, the length of time required to develop the edema, and other factors, both anatomic and pathologic, that might simulate edema of the ridge were also studied.

MATERIAL AND METHODS

Following the intravenous injection of 30 cc. of 50 per cent hypaque, two pyelograms were made at ten minutes, one with and one without ureteral pressure, in the anteroposterior projection. A posteroanterior roentgenogram was made at fifteen minutes. A coned anteroposterior bladder roentgenogram was made without angulation at twenty minutes. All the roentgen studies were made at a 40 inch distance.

The sexes were equally distributed in series of 125 patients, and the ages ranged from two to eighty-seven years. The mean age of the 105 cases in which this information was recorded was forty-five years.

Measurements of the interureteric ridge were made from the bottom of the intramural portion of the ureter filled with contrast material to the nearest point of the roof of the interureteric ridge. The roof is seen as an opaque caudally convex structure above the lucent band of the ridge. When the ureter was not visible, the thickness of the band of lucency was measured. These points were often indistinct, so the measurements are not considered to be precise. From the point of view of establishing the normal measurements, however, this is not important because, in pathologic states, the deviations from normal were quite distinct.

RESULTS

The interureteric ridge could be seen in 45 of the 125 pyelograms (36 per cent). In the 36 normal cases in which it was measurable, it averaged 5 mm., with a normal

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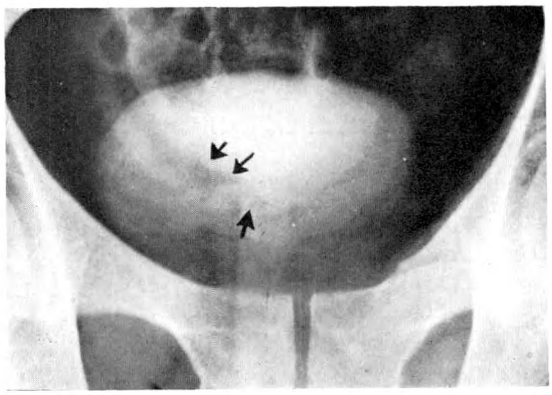


FIG. 1. H. M., a twenty-eight year old white male, had an acute onset of right flank pain and microscopic hematuria. The roentgenogram demonstrates calculus (lower arrow) and edema of the right interureteric ridge (upper arrows).

range of 2 to 9 mm. There were 12 patients with a ureterovesical stone or who had just previously passed a roentgenologically verified calculus. In 2 of these the ridge was not seen well enough to be evaluated; 8 showed edema of the ridge (Fig. 1, 2 and 3); and, in the remaining 2, in whom the studies were made five and seven days, respectively, after passage of the stones, there was no evidence of either calculus or edema. In all the cases with edema there was some retention of the contrast medium in the affected renal collecting system or complete absence of function on the affected side.

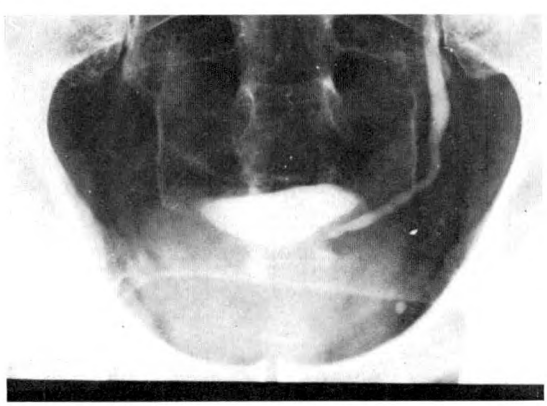


FIG. 2. J. G., a fifty-nine year old white male, had severe pain in the left lumbar region radiating to the left scrotum, and microscopic hematuria; a stone was passed spontaneously. The roentgenogram demonstrates edema of the interureteric ridge and partial ureteral obstruction.

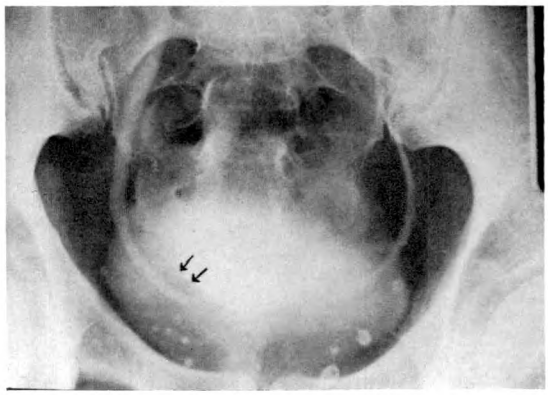


FIG. 3. P. C., a thirty-two year old white male, had severe pain in the right flank associated with frequency and microscopic hematuria; a stone was passed spontaneously. The roentgenogram indicates increased obliquity of the upper border of the interureteric ridge (arrows) associated with edema.

There was no difference in the sex distribution of those cases in which the ridge was visualized. This is contrary to Edling's results in which males predominated.

The bladder size, measured on the urograms, was graded from 1+ to 3+ in 83 cases. In 28 of these in which the ridge was visible, 19 were graded 1+ or 2+; of the remaining 55 in which the ridge was not visualized, 32 were so rated. This would appear to indicate that the ridge was visible relatively more often in those bladders that were not grossly distended. The impression was gained, confirming Edling's observations, that bladder distention was a significant factor in the failure of visualization of the interureteric ridge.

ROENTGEN ASPECTS OF THE URINARY BLADDER

The urinary bladder may present in the anteroposterior projection a number of different aspects. One may not see the interureteric ridge if the bladder is too distended or dilated. With the patient supine, stereoscopic and lateral cross-table roentgenograms show that the roof above the interureteric ridge represents the fundus of the bladder folded posteriorly over the relatively fixed trigone. The posteroanterior roentgenogram was of no assistance in the

visualization of the ridge in any instance. Oblique roentgenograms, in the few cases studied using this projection, showed the same findings as the anteroposterior roentgenograms. The opaque roof of the ridge may be confused with the edge of the overlying sacrum. The lucent interureteric ridge may be mimicked by an indentation of the inferior wall of the bladder which also casts a lucent shadow; however, it has a caudally concave lower border as compared to the convex shadow of the interureteric ridge and it always is lower in position (Fig. 4). Occasionally, the ridge may not be visualized on one examination and may be visible on another, but generally the findings are consistent on all examinations of the same patient.

When edema of the interureteric ridge is present, the affected side casts a radiolucent shadow ranging in size from 9 to 18 mm. Even more important than the width of the ridge for the recognition of edema is the alteration in the downward convexity on the affected side. Flattening and sometimes even concavity of the roof on the affected side may be quite striking. A unilateral radiolucent shadow in the region of the interureteric ridge may be caused by a ureterocele filling very slowly with contrast medium (Fig. 5). This type of defect is usually sharper in outline than edema of the ridge. It may not be accompanied by appreciable dilatation of the upper urinary tract.

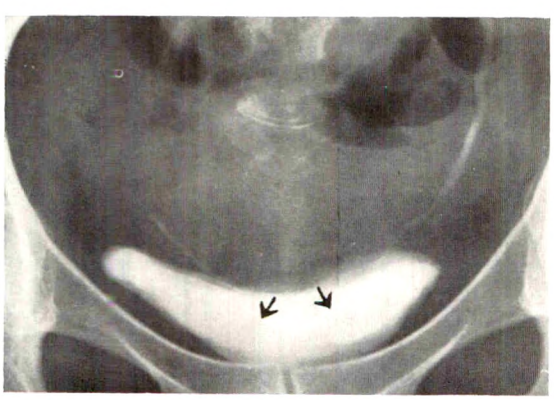


Fig. 4. The radiolucent ridge (arrows) represents an indentation of the inferior wall of the bladder. This may be confused with the interureteric ridge when the lower ureters are not visualized.

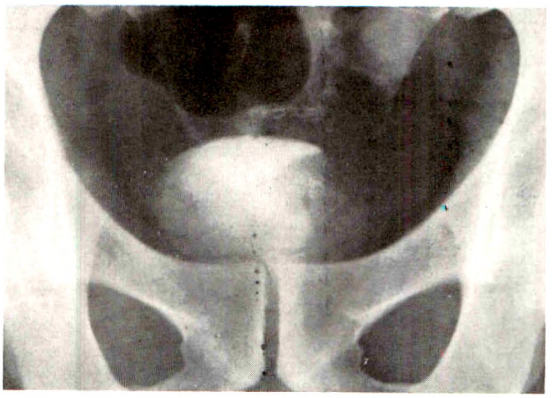


Fig. 5. J. H., a thirty-five year old white male, had pain in the left lower quadrant of the abdomen and microscopic hematuria. The roentgenogram demonstrates a ureterocele.

On occasion, extrinsic pressure from a distended intestine or from an adjacent mass lesion may cause widening of the ridge simulating the edema sign (Fig. 6). Carcinoma usually has sharper and often ragged edges.

DISCUSSION

The interureteric ridge was observed in 36 per cent of this series of 125 routine, unselected pyelograms. It was sometimes difficult to measure the ridge because the

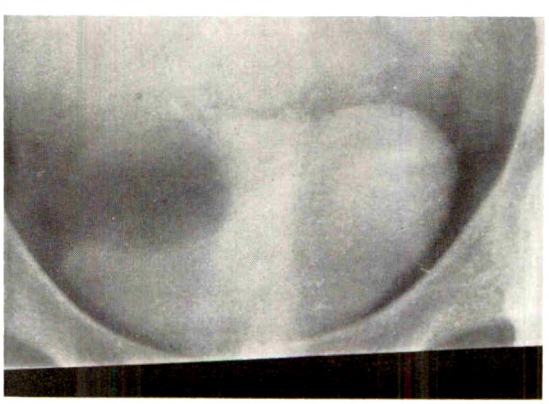


Fig. 6. E. M., a forty year old Negro female, had a palpable mass in the pelvis. The roentgenogram demonstrates extrinsic pressure on the bladder simulating edema or ureterocele. A fibroid tumor was removed and subsequent roentgen studies showed a normal appearing bladder.

roof could not be clearly seen or the distal end of the ureter was not filled with the medium. When the roof cannot be visualized the ridge cannot be measured or evaluated. In all the cases in which the ridge was visible and a calculus was present, the edema sign was evident.

The development of edema is probably rapid, since most of the roentgenograms demonstrating it were made shortly after symptoms began. However, we could not be certain how long the calculi were at the ureterovesical junction before the onset of edema. In 2 cases the edema subsided within a week; therefore, the edema sign would probably not be evident more than five days after passage of a stone.

The edema was always accompanied by other evidence of ureterovesical obstruction in the upper collecting system, such as hydronephrosis, a nephrogram or nonfunction. Hence, as an indication of ureterovesical calculus, it merely complements these other findings. The sign of edema of the ridge is most useful in the case where there is obstruction at the ureterovesical junction but where no calculus is seen. In these cases, the presence of edema would contraindicate a diagnosis of stricture, ureterocele, a fibrous band or carcinoma.

SUMMARY

Pyelograms of 125 consecutive cases were reviewed. An interureteric ridge was seen in 36 per cent. Edema of the interureteric ridge was observed in all cases of impacted or recently passed stones in which the ridge was visualized. This is a useful roentgen sign, particularly in the patient who has ureterovesical obstruction without a visible calculus.

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CHANGES IN HUMAN RED BLOOD CELLS DURING IN VITRO EXPOSURE TO SEVERAL ROENTGENOLOGIC CONTRAST MEDIA*

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THE dangerous reactions which are sometimes observed following intravascular administration of roentgenologic contrast media are poorly understood. In a recent review of the problem, Read[13] has pointed out that the mortality following cardioangiography and arteriography is very much higher than for roentgenographic procedures in which the contrast medium is administered into a peripheral vein. He reports animal experiments designed to study the direct effects that contrast media might have upon the blood itself and upon the vessels into which it flows before appreciable dilution has been effected by mixing within the circulation. Read places considerable emphasis upon the red blood cell "agglutination" that was observed microscopically in the small vascular channels close to the site of injection, and he suggests that this "agglutination" may be of major importance in the etiology of some of the serious clinical reactions.

The purpose of the present investigation has been to study *in vitro* some of the effects of various contrast media upon the human red blood cells. The report includes observations on the size, shape and agglutinability of red blood cells, penetration of contrast medium across the red blood cell membrane, and indications of red blood cell damage as evidenced by *in vitro* hemolysis and by impaired *in vivo* red blood cell survival.

METHODS

Contrast Media. Four contrast media* were studied:

Brand Name	*Composition*
urokon	sodium acetrizoate
miokon	sodium diprotrizoate
hypaque	sodium and N-methyl diatrizoate
ditriokon	sodium diatrizoate sodium diprotrizoate
"triple medium"	sodium acetrizoate sodium diprotrizoate sodium and N-methyl diatrizoate

The "triple medium" was compounded by the authors for comparative *in vitro* tests (see Fig. 4) and consisted of urokon, hypaque and miokon in final concentrations of 23.3 per cent, 25 per cent and 23.3 per cent, respectively.

Normal red blood cells were obtained from laboratory personnel known to be free from hematologic disease. Freshly drawn blood was either defibrinated with glass beads, or placed directly into acid citrate dextrose anticoagulant solution (ACD, U.S.P. Formula A). Unless otherwise stated, the blood was used within 24 hours of procurement.

Hemoglobin concentration of whole blood was determined as cyan-hemoglobin, according to Drabkin.[8] The hemoglobin concentrations in plasma or in saline wash solutions were determined by the method of Crosby and Furth[7] for levels greater than 4 mg. per 100 ml., and by the method of Hanks *et al.*[10] for levels below 4 mg. per 100 ml. It was previously determined that hemoglobin measurement by these methods was unaffected by the presence of contrast media in the solution to be tested.

Hematocrits on mixtures of red blood cells and contrast media were determined in

* Manufactured by the Mallinckrodt Chemical Works.

* From the Division of Hematology, Departments of Medicine and Preventive Medicine, Washington University School of Medicine, and the Mallinckrodt Institute of Radiology, St. Louis, Missouri.
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microhematocrit tubes (75×1.5 mm.), centrifuged for 5 minutes at 12,000 r.p.m. (approx. 9,000 g. to the midpoint of the hematocrit tube) in an International Centrifuge, model 275. Hematocrits on blood samples obtained during blood volume measurement were determined in Wintrobe tubes centrifuged for 55 minutes at 2,200 r.p.m. in a centrifuge of radius 25 cm. to the bottom of the centrifuge cups.

Mean corpuscular hemoglobin concentration (*M.C.H.C.*) was calculated in the usual manner,

$$\text{M.C.H.C.} = \frac{\text{hemoglobin, gm. per 100 ml.} \times 100}{\text{vol. packed red cells, ml. per 100 ml.}},$$

based on duplicate determinations of hemoglobin concentration and of hematocrit. Elevation in M.C.H.C. following exposure to hypertonic solutions was attributed to loss of intra-erythrocyte water.

Osmolarity was determined employing a Fiske osmometer. All samples were measured after appropriate dilution to provide levels of approximately 300 m.osm./per kg. of H_2O.

Specific gravity of concentrated solutions of contrast media was determined by triplicate weighing of accurately measured 5 ml. volumes and comparison against distilled water weighed under identical conditions.

Quantitative Measurement of Intracellular Penetration of Contrast Medium. Six 12 ml. aliquots of fresh defibrinated blood were centrifuged for 1 hour at 2,200 r.p.m.; the supernatant plasma and upper red blood cell layers were aspirated so as to leave 5.0 ml. of packed red blood cells remaining in each tube. Under these conditions it is known[5] that trapped saline makes up <2 per cent of the packed cell mass. Sufficient I^{131}-tagged urokon* was added to each of three urokon solutions (final urokon concentrations 2 per cent, 10 per cent, 20 per cent) to provide a convenient counting rate. To each of two tubes containing 5 ml. of packed red blood cells was added 5 ml. of a tagged urokon solution. The contents were thoroughly mixed; after room temperature incubation of one tube for 5 minutes, the other for 30 minutes, aliquots were removed for measurement of hemoglobin and hematocrit and the tubes were centrifuged for 40 minutes at 2,200 r.p.m. The penetration of urokon into the cells was determined from the decrease in radioactivity of the supernatant fluid obtained after centrifugation compared with the original urokon solution. Appropriate corrections for the shift of water out of the cells were made on the basis of M.C.H.C. values determined on the original red blood cells and on the aliquots removed after the 5 and 30 minute periods of incubation. Intracellular water was assumed to equal 65 per cent of the true original red blood cell mass. Radioactivity was measured in a well-type scintillation counter.

In vivo red cell survival was determined using Cr^{51}, essentially as described by Ebaugh and co-workers.[9] After exposure for 30 minutes to 50 μc of Cr^{51} as sodium chromate, tagged normal red blood cells were incubated with the contrast media and then washed three times with 20 volumes of saline. Ten milliliters of tagged red blood cell suspension were injected from a calibrated syringe. Expected immediate 100 per cent survival was estimated as:

$$\text{expected counts per ml. of recipient's blood} = \frac{\text{total counts injected}}{\text{blood volume (ml.)}}.$$

Plasma volume was measured by the Evans Blue dye method, and blood volume calculated employing the hematocrit corrected for plasma trapping[5] and for the body/venous hematocrit ratio.[6]

RESULTS

Gross Observations. When a volume of whole blood was mixed with an equal volume of any of the four concentrated (*e.g.*, 70 per cent) contrast media, there was no immediate aggregation of red blood cells visible grossly or microscopically. However, after the mixture had stood undisturbed for

* Supplied by Abbott Laboratories.

several minutes, aggregates of red blood cells were observed in the film of blood on the wall of the tube above the fluid level. If the mixture was allowed to stand undisturbed for periods up to 1 hour, the clumps of red blood cells increased in number and in size. Mixing of the contents by repeated inversion of the test tube caused rapid dispersion of the red blood cell aggregates. When the mixtures were centrifuged after varying intervals of incubation, the red blood cells migrated to the top of the fluid layer and adhered together in a "slime" which broke up into smaller aggregates following vigorous remixing (Fig. 1). Progressively severe hemolysis was observed in the underlying fluid following centrifugation, depending on the length of incubation of the mixtures. The spontaneous aggregation of red blood cells was independent of the presence of plasma and could be largely prevented by repeated slow inversion of the tube during the first 5 to 10 minutes following addition of the blood to the contrast medium. Spontaneous clumping of red blood cells did not occur during subsequent undisturbed incubation, but comparable hemolysis was observed after centrifugation of the mixtures, and the centrifuged red cells formed an overlying "slime," as previously. It therefore appeared that spontaneous aggregation of red blood cells was favored if they were left undisturbed immediately following contact with high concentrations of contrast medium, presumably during the period of acute changes in the cells' size and surface properties. Once the red blood cells achieved a relatively "steady state," the forces of mutual attraction were greatly diminished and were manifested only when the red blood cells were brought into close contact by centrifugal force. The phenomenon of red blood cell lysis was largely independent of the aggregation, since it was of comparable severity in mixtures in which clumping was prevented by gentle motion of the test tube.

Microscopic Observations. Immediately upon exposure to high concentrations of contrast medium, the red blood cells examined in a free drop of fluid lost their biconcave shape and appeared initially as flat irregular plates or small dense spheres. When examined in a thin layer under a glass cover slip, all of the cells appeared as small dense spheres. After a sufficient period of exposure, hemolysis of cells occurred as evidenced by rapid fading of the cell color, leaving a faintly visible shrunken ghost. When an aggregate of adherent red blood cells was examined in a free drop of contrast medium, large numbers of cells were seen congregated together in tangential contact, but without the close approximation of cell walls and without the cellular distortion characteristic of immune agglutination. There was no rouleau formation. The application of a glass cover slip caused complete dispersion of all but the largest aggregates, indicating the weakness of the forces responsible for the aggregation. When red blood cells were exposed to solutions of NaCl, $Na_3C_6H_5O_7$ or dextrose of osmolarities equivalent to the concentrated contrast media, entirely similar changes in cell size, shape and properties of adherence were observed, but without significant hemolysis, even when exposure was extended over a period of several hours.

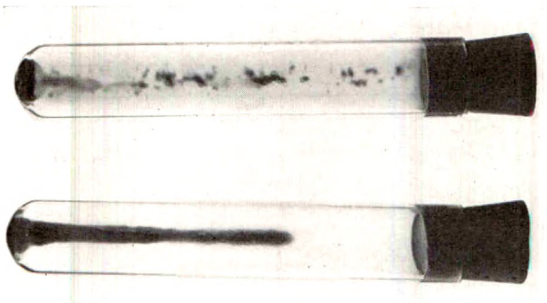


Fig. 1. Red blood cell aggregation following exposure to concentrated contrast medium. The red blood cells in the upper tube were exposed to urokon, centrifuged lightly and resuspended by inversion of the tube. Note the irregular cellular aggregates; the gray background is in part due to hemolysis. Evenly dispersed control cells suspended in saline are shown in the lower tube; the clear background indicates absence of hemolysis.

Reversibility of Morphologic Changes. The

concentrated contrast media were removed by washing the red blood cells three times in 20 volumes of isotonic sodium chloride solution. Striking further hemolysis of cells occurred during the first two washes, diminishing with the third wash (see ahead for quantitation of hemolysis). When the washed cells were resuspended in their native plasma, most of them regained their original size and biconcave shape and formed rouleau normally. However, the longer the period of exposure to the concentrated contrast media, the greater the number of cells which remained as small dense refractile spheres, suggesting irreversible damage.

Agglutinability of Cells. On several occasions, red blood cells from a group A_1 donor were exposed for various periods to concentrated contrast media, then washed three times, and the recovered cells made up to an accurate 2 per cent suspension in saline and compared with a 2 per cent suspension of unexposed cells against multiple dilutions of an anti-A serum. There was no evidence of impaired agglutinability of the recovered cells (a representative result is shown in Table I).

Quantitative Evidence for Cell Shrinkage. Five milliliter volumes of packed washed red blood cells were mixed with equal volumes of 14 per cent, 20 per cent and 26 per cent solutions of urokon. Samples were removed for duplicate hemoglobin and microhematocrit determinations after 5, 15 and 30 minutes of incubation. Progressive shrinkage of the red blood cells was observed as indicated by the rises in mean corpuscular hemoglobin concentration (M.C.H.C.) shown in Table II. Attempts to extend these observations to higher concentrations of the contrast medium were frustrated by the high density of the medium, which prohibited satisfactory sedimentation of the red blood cells by centrifugation. However, Figure 2 indicates that similar changes occurred in red blood cells exposed to somewhat higher concentrations of contrast media. Initially the red blood cells (specific gravity approximately 1.095) floated on top of the media. However, during incubation, loss of water from the red blood cells due to osmotic shrinkage resulted in increased cellular specific gravity and decreased specific gravity in the suspending medium, which favored an increasing number of cells being driven to the bottom of the hematocrit tube by centrifugal force. The calculated changes in intracellular and extracellular specific gravities occurring in response to the shift

Table II

RED BLOOD CELL SHRINKAGE DURING EXPOSURE TO CONTRAST MEDIUM

Concentration of Urokon	M.C.H.C.* (per cent) after incubation			
	Control	5 min.	15 min.	30 min.
14%	32.5	33.5	33.9	35.4
20%	32.5	34.2	35.3	40.5
26%	32.5	35.8	40.0	42.6

* Mean corpuscular hemoglobin concentration.

Table I

AGGLUTINABILITY OF RED BLOOD CELLS AFTER EXPOSURE TO CONTRAST MEDIUM

	Dilutions of Anti-A Serum							
	1/1	1/2	1/4	1/8	1/16	1/32	1/64	1/128
A_1 control cells	4	4	4	3–4	3	2	1	±
A_1 cells recovered after exposure to 40% urokon for 40 minutes	4	4	4	3–4	3	2–3	1	1

CONTRAST MEDIUM			INCUBATION PRIOR TO CENTRIFUGATION			
	Osmolarity	Spec. Grav.	5 mins.	10 mins.	15 mins.	30 mins.
UROKON 40%	1290 m. osm.	1. 269				
DITRIOKON 39%	1120 m. osm.	1. 247				
HYPAQUE 41%	1000 m. osm.	1. 234				

FIG. 2. Sedimentation of red blood cells by centrifugation after increasing periods of exposure in three contrast media. Blocks are diagrammatic representations of hematocrit tubes following centrifugation at 9,000 g. Note that following short periods of incubation the centrifuged red blood cells remain near the top of the tube; as the incubation period is prolonged, increasing numbers of cells can be centrifuged to the bottom of tube. The gray background represents increasing hemolysis with longer periods of incubation.

of water out of the cells were insufficient to account for the successful sedimentation of red blood cells in the relatively high concentrations of contrast media. It therefore seemed likely that some of the relatively heavy contrast medium had penetrated inside the cells.

Evidence that Urokon Penetrates Red Blood Cells. Fresh red blood cells were incubated for 45 minutes with equi-osmolar solutions of urokon, sodium chloride (a penetrating salt), trisodium citrate (a non-penetrating salt) and dextrose (which penetrates the red blood cell membrane, but does not come to complete equilibrium at high dextrose concentrations). The results, summarized in Table III, illustrate that the highest M.C.H.C. (44.6 per cent), indicating the greatest red blood cell shrinkage, was observed in the solution containing the citrate ion, to which the red blood cell membrane is impermeable. By contrast, the shrinkage of red blood cells in the solution containing urokon resembled that observed in the solutions containing the penetrating dextrose molecule and chloride ion.

Quantitative measurement of penetra-

TABLE III

SHRINKAGE OF RED BLOOD CELLS FOLLOWING 45 MINUTES INCUBATION IN FOUR HYPERTONIC SOLUTIONS

	Osmolarity (m.osm. /kg.H_2O)	M.C.H.C.* (per cent)
20% urokon	630	35.6
1.84% NaCl	630	37.7
10.8% dextrose	630	34.9
6.56% $Na_3C_6H_5O_7 \cdot 5\frac{1}{2}H_2O$	630	44.6

* Mean corpuscular hemoglobin concentration.

TABLE IV

PENETRATION OF UROKON ACROSS THE RED BLOOD CELL MEMBRANE

	Incubation (min.)	Intracellular Urokon Concentration (I.U.C.) (per cent)	Extracellular Urokon Concentration (E.U.C.) (per cent)	Ratio I.U.C./E.U.C.
2% urokon	5	0.25	1.8	0.139
	30	0.28	1.79	0.156
10% urokon	5	2.62	7.9	0.332
	30	2.75	7.68	0.358
20% urokon	5	6.0	14.9	0.402
	30	6.6	14.3	0.462

tion was accomplished employing I^{131}-tagged urokon, as described in detail under Methods. Observations were made after 5 and 30 minutes' incubation of red blood cells in final urokon concentrations of 2 per cent, 10 per cent and 20 per cent. The results are summarized in Table IV, where it is evident that the contrast medium penetrated into the red blood cells and that most of the penetration occurred within the first 5 minutes of exposure. The 0.139 and 0.156 ratios of intracellular and extracellular urokon concentration at an initial urokon concentration of 2 per cent indicate the maintenance of a steep gradient across the cell membrane; the higher ratios (0.332 and 0.402) obtained with the 10 per cent and 20 per cent concentrations of urokon may be indicative of progressive red blood cell damage. No attempt was made to extend these studies to urokon concentrations higher than 20 per cent because of the difficulty of accurate determination of M.C.H.C. at the high specific gravities of the more concentrated urokon solutions, and because gross hemolysis indicated profound cellular damage.

The red blood cells exposed to 10 per cent tagged urokon were subsequently washed three times with untagged 10 per cent urokon. Considerable exchange of the intracellular tagged urokon occurred during the washing procedure, but at the conclusion of the third wash it was determined that the intracellular concentration of urokon I^{131} was three times greater than in the supernatant wash solution.

Quantitation of Hemolysis. When red blood cells were exposed to high concentrations of contrast media, increasing hemolysis occurred with increasingly long periods of exposure. When the red blood cells were replaced in a physiologic medium (*e.g.*, plasma, or 0.85 per cent NaCl), further hemolysis occurred. To illustrate the extent of the hemolysis, packed washed red blood cells were incubated with an equal volume of contrast medium for 40 minutes, then washed three times with 20 volumes of 0.85 per cent NaCl solution. The total free hemoglobin in each wash solution was measured and expressed as a percentage of the total hemoglobin present in the original intact red blood cell mass. In Figure 3, three contrast media adjusted to the same osmolarity (1830 m.osm./kg. H_2O) are compared with equi-osmolar

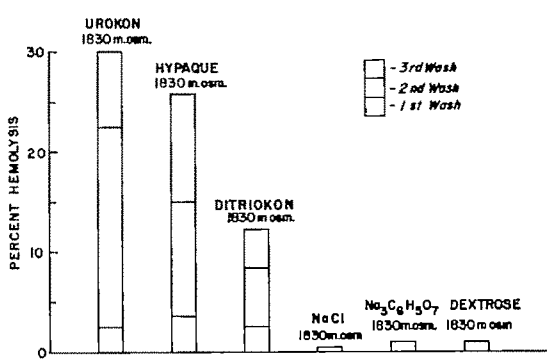


FIG. 3. Hemolysis following 40 minutes exposure to equi-osmolar solutions. The hemoglobin present in each wash solution is expressed as a per cent of the total hemoglobin present in the original red blood cell mass. There was so little hemolysis following exposure to equi-osmolar solutions of NaCl, $Na_3C_6H_5O_7$ and dextrose that the results of three washes were combined in drawing the three blocks on the right.

solutions of NaCl, $Na_3C_6H_5O_7$ and dextrose. Evidently, there are substantial differences between contrast media as to their ability to damage red blood cells as manifested by hemolysis (compare urokon and ditriokon). Furthermore, the hemolytic effect is much in excess of what could be attributed to their hypertonicity; for minimal hemolysis occurred when red blood cells were exposed to equi-osmolar solutions of NaCl, $Na_3C_6H_5O_7$ and dextrose. In Figure 4, similar observations are recorded for urokon, ditriokon and hypaque in concentrations supplied for use in clinical angiography. In addition, there are shown the effects of 70 per cent miokon (usually supplied as a 50 per cent solution because of its relative insolubility). On the extreme right is shown a "triple medium" composed of urokon, hypaque and miokon in final concentrations of 23.3 per cent, 25 per cent and 23.3 per cent, respectively. When the latter medium and ditriokon (which is a combination of hypaque 36.7 per cent and miokon 31.4 per cent) are compared with urokon, it is apparent that hemolysis may be diminished in the presence of combinations of organic iodide compounds, where no single compound is present in very high concentration. Finally, Figure 5 illustrates the extent to which hemolysis is dependent on the concentration of the contrast medium. Less than 5 per cent hemolysis occurred after 40 minutes of exposure to 33 per cent urokon, but hemolysis exceeded 80 per cent after comparable exposure to 50 per cent urokon.

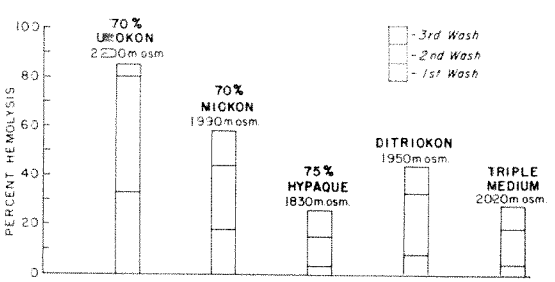


FIG. 4. Hemolysis following 40 minutes exposure to concentrated contrast media. The relatively small amount of hemolysis observed with the "triple medium" (which contains 23.3 per cent urokon, 23.3 per cent miokon and 25 per cent hypaque) may indicate a less damaging effect of combined contrast media, in which no single medium is present in high concentration.

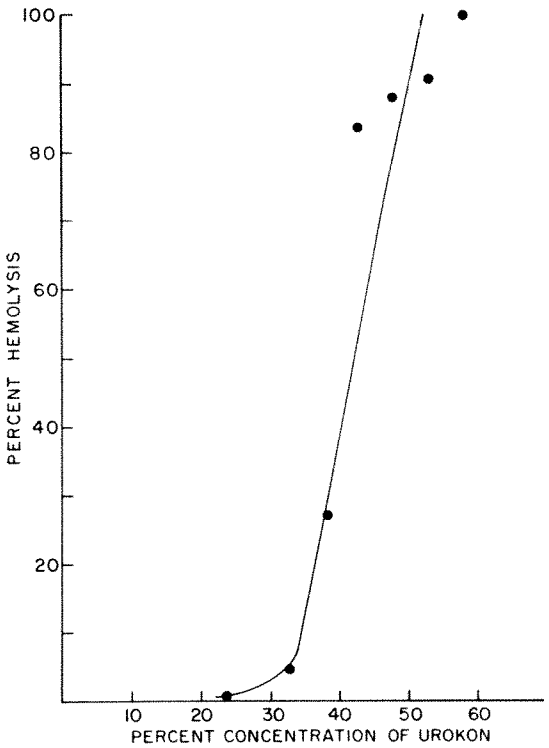


FIG. 5. Relation of hemolysis to concentration of urokon. Points on the curve represent the combined hemolysis occurring in three washes following 40 minutes exposure to urokon.

The extent to which hemolysis occurs following the clinical use of concentrated contrast media must be very small. On four occasions, samples of venous blood were collected within 20 minutes of completion of clinical angiographic studies, and in no instance did the plasma hemoglobin concentration exceed 0.7 mg. per 100 ml. These findings indicate negligible intravascular erythrocyte destruction (*i.e.*, certainly less than 0.25 ml. of red blood cells).[4]

Effect of Urokon on Red Blood Cell Viability. Normal red blood cells tagged with Cr^{51} were exposed to 45 per cent urokon for 1 minute on one occasion and for 45 minutes on another occasion; thereafter they

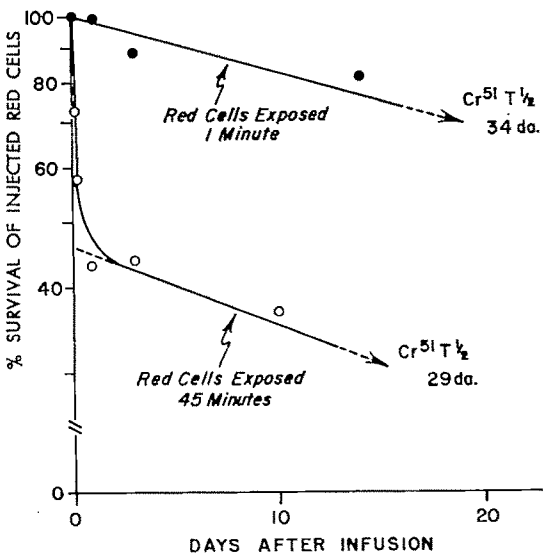


FIG. 6. *In vivo* survival of red blood cells recovered after exposure to 45 per cent urokon. During exposure and three subsequent saline washes prior to undertaking the *in vivo* survival studies, there was approximately 10 per cent hemolysis of the cells exposed to urokon for 1 minute and 50 per cent hemolysis of cells exposed to urokon for 45 minutes.

were washed 3 times with saline, resuspended in plasma and reinjected into the original donor (see Methods). The cells exposed to urokon for only 1 minute underwent approximately 10 per cent hemolysis prior to injection (*i.e.*, during exposure and washing), as compared to approximately 50 per cent hemolysis of the cells exposed for 45 minutes. The *in vivo* survivals of the injected cells are shown in Figure 6. Evidently there was no serious damage to the cells which were not hemolyzed during 1 minute's exposure to urokon and the subsequent washing procedure; they exhibited the expected 100 per cent immediate survival, and the Cr^{51} $T\frac{1}{2}$ followed over the succeeding 13 days was entirely normal (34 days). However, of the injected cells recovered after exposure to urokon for 45 minutes only 73 per cent were present in the circulation 10 minutes after injection, 58 per cent three hours after injection and 43 per cent 21 hours after injection. Not all of the cells were irreversibly damaged, for those which were present at 21 hours went on to survive normally as observed over the ensuing 12 days (Cr^{51} $T\frac{1}{2}$ 29 days).

Observation of the Rabbit Nictitating Membrane after Intracarotid Injection of Urokon. Injections were made into the cannulated carotid artery of the nembutalized rabbit, with continuous observation of arterioles, capillaries and venules employing a Zeiss slit lamp with green filter at 16× magnification. There is normally an irregular pulsatile pattern in the membrane vessels, and some segmentation of the red blood cell column is normally observed when the flow through a particular vessel complex is temporarily slowed. Sterile pyrogen free physiologic saline was injected rapidly in amounts of 0.2, 0.4, 0.8 and 1.0 ml. The only effect, observed mainly following the larger injections, was moderate temporary (30–60 seconds) spasm of the arterioles, with consequent slowing of flow in the capillaries and collecting venules and with accompanying segmentation of the red blood cell column during the intervals of retarded flow. Injection of 70 per cent urokon, even in amounts of 0.2 and 0.4 ml., was generally accompanied by an irritative reaction consisting of transient generalized muscular contractions, associated with more severe and prolonged spasm of the membrane arterioles. When 0.8 and 1.0 ml. of 70 per cent urokon were injected, the rabbit often experienced a generalized convulsion. Again, during periods of retarded blood flow secondary to arteriolar spasm, segmentation of the red blood cell column in the capillaries and venules was observed. However, as soon as the arterioles resumed their normal diameter (after 1 to 3 minutes), normal blood flow was promptly reestablished. The observers saw no evidence of sludging, or "agglutination" of the red blood cells that could be definitely attributed to a direct effect of the urokon causing *in vivo* intravascular aggregation of the cells.

DISCUSSION

The physiologic mechanisms underlying untoward clinical reactions to roentgenologic contrast media remain somewhat obscure. While some of the reactions (*e.g.*, urticarial) are almost certainly allergic in origin, others (*e.g.*, hemiplegia) appear to result from damage to areas in which the vascular supply is in the direct route of the injected material. The present investigation throws no light on the problems of allergic reactions; its purpose has been to explore possible ways in which the contrast media might cause direct damage to intact viable cells.

The human erythrocyte can be considered a relatively "tough" cell by comparison to most other soft tissue cells. It withstands refrigerated storage outside the human host for 3–4 weeks in relatively simple preservative solutions without great loss of viability. It is able to withstand striking changes in cell volume due to gain or loss of water, a property related in part to its existence as a "free cell" without intimate attachment to adjacent cells, and in part to its unique spatial form as a biconcave disk. It is interesting therefore to consider the changes in size, shape, membrane characteristics, and viability brought about after exposure to contrast media in current clinical usage.

Fresh erythrocytes were employed throughout the present investigation, for it was observed that stored red blood cells exhibited increased susceptibility to cellular aggregation and more rapid and extensive hemolysis than fresh red blood cells tested under identical conditions. The effects of the concentrated contrast media were manifested rapidly, as evidenced by the acute shrinkage of the red blood cells (observed microscopically to occur within seconds), the relatively prompt penetration of the organic iodide compound across the red blood cell membrane (Table IV), and the hemolysis (up to 10 per cent) that occurred when exposure was allowed for only 1 minute and then terminated by rapid dilution and repeated washing in physiologic saline solution. Undoubtedly some of the hemolysis observed during the washing procedures reflected the "paradoxical hypotonic hemolysis" discussed by Soderstrom,[15] and encountered so dramatically during the washing of red blood cells which had been suspended in high concentrations of penetrating polyhydric alcohols.[3,11] When intracellular osmolarity has been elevated by suspending cells in hypertonic solutions of a substance capable of penetrating across the cell membrane, sudden re-exposure of the cells to "physiologic" osmolarity may result in extremely rapid entry of water into the cells so that they swell and burst. This type of hemolysis can be largely eliminated by very slow addition of the physiologic wash solution, thereby permitting a gradual lowering in the osmolarity of the suspending fluid and allowing establishment of equilibrium between intracellular and extracellular solute. However, when physiologic saline was added very slowly to red blood cells which had been suspended in concentrated contrast media, only a modest decrease in hemolysis was achieved, suggesting that osmotic effects were not primarily responsible for the observed hemolysis. The failure of comparably hypertonic sodium chloride, sodium citrate and dextrose solutions to provoke significant hemolysis (Fig. 3) constitutes further evidence that the damage caused by concentrated contrast media results from other than simple osmotic effects. The diminished red blood cell survival illustrated in the lower curve on Figure 6 further documents the extent of the red blood cell damage; and provides an interesting avenue for further investigation into the cause for normal *in vivo* survival of a small proportion of the injected cells. Other observations which merit further study are the discrepancies in hemolytic potential among different contrast media (illustrated in Fig. 3) and the suggestion that hemolytic potential

may be decreased by employing "combined" contrast media (*e.g.*, ditriokon, hypaque, "triple medium") in which the total iodine content is high but in which no single organic iodide is present in high concentration. The importance of the stability of organic iodide "combinations" deserves special emphasis. For example, the "triple medium," which caused relatively little hemolysis when freshly prepared (Fig. 3), was noted to darken in color during 3 weeks' storage at summer room temperatures and when retested proved to be almost as hemolytic as the 70 per cent urokon over which it had excelled previously.

It remains an open question whether serious reactions to roentgenologic contrast media may result from aggregation of red blood cells, with secondary vascular plugging, or from a direct toxic effect of the media upon the vessel wall itself, particularly upon the endothelium. Mudd and his co-workers[12] have demonstrated what they describe as "agglutinative thrombosis" within small pulmonary vessels in stained sections of lung tissue obtained from dogs within 1 to 60 minutes after injection of 70 per cent urokon into the pulmonary artery. Similar findings have been described by Read and co-workers,[14] who made direct observations of small pial and mesenteric vessels following the rapid intra-arterial injection of hypertonic solutions (20 per cent NaCl, 50 per cent glucose). In another report, Read[13] has stressed the important role of the red blood cell in causation of the pulmonary hypertension that is observed following injection of concentrated contrast media into the pulmonary artery; for when the isolated lung was perfused with contrast media alone, elevation of pulmonary arterial pressure did not occur.

The present authors do not deny the possibility that intravascular aggregation of red blood cells may be important as a cause of clinical reactions. However, we were impressed by the fact that: (1) red cell clumping did not occur as long as the blood and contrast media were kept in motion; (2) clumping might be expected to occur *secondary* to greatly retarded blood flow, as appeared to be the case in the studies on rabbit nictitating membrane; and (3) the red blood cell clumps did not resemble tightly adherent immune red blood cell agglutinates, but rather represented a tangential aggregation of cells which could be easily dispersed when the stagnant red blood cell suspension was put back in motion. Also impressive were the evidences for direct damage to the red blood cell: hemolysis far exceeding what would be expected from the hypertonicity of the media, and impaired viability of over half of the red blood cells recovered after *in vitro* exposure to contrast medium. It seems certain that the exposed vascular endothelium must undergo somewhat similar changes to those observed in the red blood cell, and it might be expected that the anatomy of the endothelium would make it more susceptible than the red blood cell to some of the damaging effects of the media. Evidence for direct vascular damage has been reported by Zinner and Gottlob[16] and evidence for altered vascular permeability has been presented by Broman and Olsson.[1,2]

Whatever may be the actual mechanism(s) underlying nonallergic clinical reactions to contrast media, the present studies indicate that the red blood cell may serve as a convenient model for describing some of the properties of existing and newly developed media. It remains to be seen whether evidence of damage to red blood cells will be paralleled by a high incidence of serious clinical reactions. However, it would seem to be worthwhile to attempt a correlation of *in vitro* red blood cell findings with large scale clinical trials as a further adjunct in the continuing development of safer roentgenologic procedures.

SUMMARY

1. Four roentgenologic contrast media were studied for their *in vitro* effects upon fresh normal human erythrocytes.

2. In the presence of high concentrations of contrast media, red blood cells underwent rapid shrinkage and exhibited a tendency to clump in loosely adherent aggregates. Aggregates could be easily dispersed by gently mixing, and initial red blood cell aggregation could be largely prevented by keeping the blood in motion following exposure to contrast media.

3. Rapid penetration of contrast medium across the red blood cell membrane was demonstrated employing I^{131}-tagged urokon.

4. Concentrated contrast media were capable of directly damaging red blood cells, as evidenced by (a) hemolysis in excess of that expected due to osmotic effects alone and (b) impaired *in vivo* survival of a proportion of red blood cells recovered after *in vitro* exposure to one of the media.

5. Observations of the small vessels in the rabbit nictitating membrane following intracarotid injection of 70 per cent urokon were inconclusive but did not provide evidence of primary intravascular clumping of erythrocytes.

6. The possible value of attempting to correlate the *in vitro* effects of contrast media upon red blood cells and the *in vivo* incidence of nonallergic clinical reactions is discussed.

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EXPERIMENTAL STUDIES OF DITRIOKON TOXICITY*

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IN VIEW of the development of cardiovascular diagnostic procedures which utilize large volumes of concentrated angiographic agents, the availability of preparations with a high degree of radiopacity, low toxicity, and ease of rapid administration has become important. Factors involved in the suitability of such preparations include the immediate cardiorespiratory effects, renal and nervous system effects, and those effects due to such physicochemical properties as viscosity and osmolality.

The recent combination of sodium diprotrizoate and diatrizoate, marketed as ditriokon,* is an attempt to provide a preparation with a high degree of radiopacity and low viscosity. It seemed worthwhile to evaluate this preparation experimentally for possible utilization in forward angiographic procedures requiring large doses of radiopaque materials.

ACUTE ANIMAL TOXICITY STUDIES

A. MATERIALS AND METHODS

Mongrel dogs of both sexes weighing from 5.5 to 10.9 kg. were anesthetized with sodium pentobarbital. Aortic blood pressure was monitored by means of a catheter in the proximal descending thoracic aorta connected to a Statham P23D strain gauge and recorded on a Sanborn Twin-Viso recorder. Lead II of the electrocardiogram was also monitored on this recorder. Observations were made of the microcirculation of the bulbar conjunctiva, of the presence and duration of apnea following injection, and of survival.

Ditriokon† was administered in graded doses from 3 to 7 cc. per kg. body weight, through a No. 280 polyethylene tube inserted into the vena cava via the femoral vein. Injection was made with the aid of a steel syringe and a hand lever injector, and in all instances the time required for injection was less than 1.5 seconds. Three dogs were injected at each dose level. Animals which survived for twenty minutes with normal vital signs were sacrificed, and, together with all animals which succumbed, were autopsied.

B. RESULTS

A summary of the results of the acute animal toxicity studies is presented in Table 1. In general, doses of 3 and 4 cc. of ditriokon per kg. body weight were well tolerated. There were some ST and T wave changes on the electrocardiogram but these were, in general, rapidly reversed. In a number of these animals, there was a short period of initial hypertension, uniformly followed by a period of hypotension. At the 3 cc. per kg. dose, the maximum systemic diastolic blood pressure drop ranged from 33 per cent to 50 per cent of the pre-injection values. At 4 cc. per kg., the maximum systemic diastolic blood pressure drop ranged from 70 to 91 per cent of the control values.

As the dose of ditriokon was increased to 5, 6, and 7 cc. per kg., the electrocardiographic and blood pressure changes became more severe. The presence of an atrial T wave, and severe S-T changes were accompanied by marked and irregular bradycardia, apparently of sinus origin. The post-injection phase of hypotension was uniformly profound (see Table 1).

Observations of the small blood vessels

* Mallinckrodt Chemical Works.

† Generously supplied by Mallinckrodt Chemical Works, St. Louis, Missouri.

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† Post-Doctoral Research Fellow, National Heart Institute, United States Public Health Service.
‡ Assistant Professor, Department of Physiology.

TABLE I

SUMMARY OF ACUTE ANIMAL TOXICITY DATA FOLLOWING MASSIVE INTRAVENOUS DOSES OF DITRIOKON

Dose (cc./kg.)	Weight (kg.)	Survival	Electrocardiographic Analysis			Blood Pressure Change		Pulse Pressure		Maximum Diastolic Blood Pressure Drop (%)	Red Blood Cell Aggregation	Pulmonary Pathology			
			Rhythm	Rate	Ischemic Changes	<5 sec.	>5 sec.	Initial	Max. Recovery	$\frac{-\Delta P_D}{P_D} \times 100$	Bulbar Conjunctiva	Hemorrhage	Edema	Dilated Capillaries	Dilated Veins
3	7.3	Yes	Reg.	—	3	Incr.	Decr.	25	40	48	2+	2+	—	2+	2+
	5.4	Yes	Reg.	—	2, 3	Incr.	Decr.	40	50	33	0	—	—	1+	—
	9.6	Yes	Reg.	—	3	—	Decr.	30	50	50	2+	—	—	2+	—
4	8.2	Yes	Irreg.	Decr.	2, 3	Incr.	Decr.	45	110	70	2+	1+	1+	1+	—
	10.9	Yes	Irreg.*	Decr.	1, 2, 3	Decr.	Decr.	40	55	91	2+	—	—	2+	—
	9.1	Yes	Reg.	Decr.	1, 2, 3	Decr.	Decr.	25	50	75	3+	—	—	—	1+
5	8.7	Yes	Irreg.*	Decr.	1, 2, 3	Decr.	Decr.	55	90	95	+	—	—	2+	—
	5.5	Yes	Reg.	Decr.	1, 2, 3	Decr.	Decr.	35	40	95	+	—	—	2+	—
	8.2	Yes	Reg.	—	2, 3	Decr.	Decr.	35	65	88	2+	1+	—	1+	—
6	5.5	Yes	Reg.	Decr.	2, 3	Decr.	Decr.	70	75	78	+	1+	—	2+	2+
	10.5	No	Irreg.*	Decr.	2, 3	Decr.	Decr.	30	—	100	3+	1+	—	4+	4+
	9.6	Yes	Irreg.	Decr.	1, 2, 3	Decr.	Decr.	45	70	83	3+	1+	—	1+	—
7	7.3	No	Irreg.	Decr.	2, 3	Decr.	Decr.	60	—	100	4+	2+	2+	1+	3+
	7.3	No.	Reg.	Decr.	2, 3	Decr.	Decr.	40	—	100	4+	2+	1+	3+	3+
	6.4	No	Irreg.	Decr.	1, 2, 3	Decr.	Decr.	35	—	100	4+	3+	3+	2+	2+

* Dropped beats.
1—Atrial T wave.
2—ST depression.
3—T wave elevation.

of the bulbar conjunctiva revealed the presence of some red blood cell aggregation in almost all of the dogs following ditriokon injection. In general, there was some correlation between the dose of ditriokon administered and the degree of aggregation visualized.

In the dogs receiving 3 cc. of ditriokon per kg., there was little or no respiratory arrest following injection (Table I). This is in marked contrast to the normal 30 to 40 second period of apnea which follows the injection of an equal volume of hypaque 90 per cent in the dog.[1] With larger injections of ditriokon, apnea appeared and became progressively longer with increased dosage.

At autopsy, in the 3 and 4 cc. per kg. dose range, most animals had minimal areas of pulmonary hemorrhage, or dilatation of pulmonary capillaries and/or veins. As the dosage of ditriokon was increased, the appearance of localized areas of pulmonary hemorrhage was common. However, dilated pulmonary capillaries and veins were the most prominent and consistent histologic findings at all dose levels tested. Histologic sections of the heart, liver, pancreas, spleen, small intestine, and kidneys of all of the animals studied failed to reveal any other significant pathology.

A comparison of the mortality subsequent to massive intravenous doses of ditriokon and hypaque 90 per cent (as reported previously[1]) is shown in Figure 1.

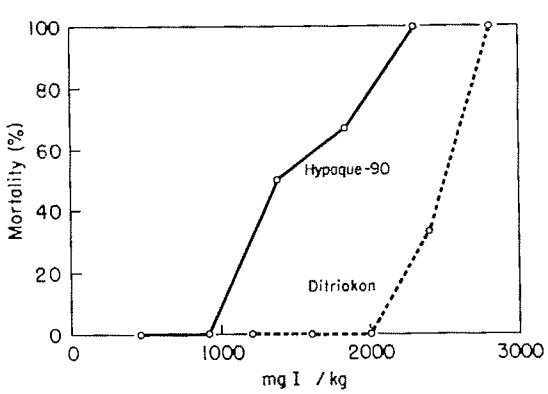


FIG. 1. Dose-mortality curve following rapid intravenous injections of ditriokon (40 mg. I/cc.) and hypaque 90 per cent (46 mg. I/cc.) in the dog.

It may be noted that mortality has been plotted against milligrams of iodine delivered per kg. body weight, rather than in terms of volume of media. It is felt that this is a more equitable way of comparing opacification ability with mortality.

Several examples of the blood pressure and electrocardiographic response to massive doses of ditriokon are shown in Figures 2, 3, and 4. At a dose of 3 cc. per kg., it may be seen that there are essentially no changes in cardiac rate or rhythm, and minor and rapidly reversible T wave changes in the electrocardiogram (Fig. 2). When the dose is increased to 6 cc. per kg., an initial hypertension, accompanied by prompt S-T segment changes, is followed by a severe sinus bradycardia, profound hypotension, and death (Fig. 3). A similar pattern, shown in Figure 4, was recorded in an animal receiving 7 cc. of ditriokon per kg. Electrocardiographic changes in the animals receiving very large doses of ditriokon are seen within 1–2 seconds of the start of injection. Some direct toxic action or reflex mechanism involving the sino-atrial node appears to be involved.

PHYSICOCHEMICAL STUDIES

A. OSMOLALITY

Determinations of the osmolality of a number of commonly employed angiographic media were performed using a Fiske osmometer,* which employs the freezing point depression principle. The studies are summarized in Table II, in comparison to normal blood osmolality, and indicate the relative hypertonicity of the substances studied. There is a good correlation between the osmolality and the amount of iodine in the compounds studied.

These studies are of particular interest in view of the recent report which implicates osmolality as one of the most important factors in the subsequent development of red blood cell aggregation and hemodynamic alterations following the rapid injection of these agents.[3] Ditriokon

* Through the cooperation of Dr. Theodore R. Grage.

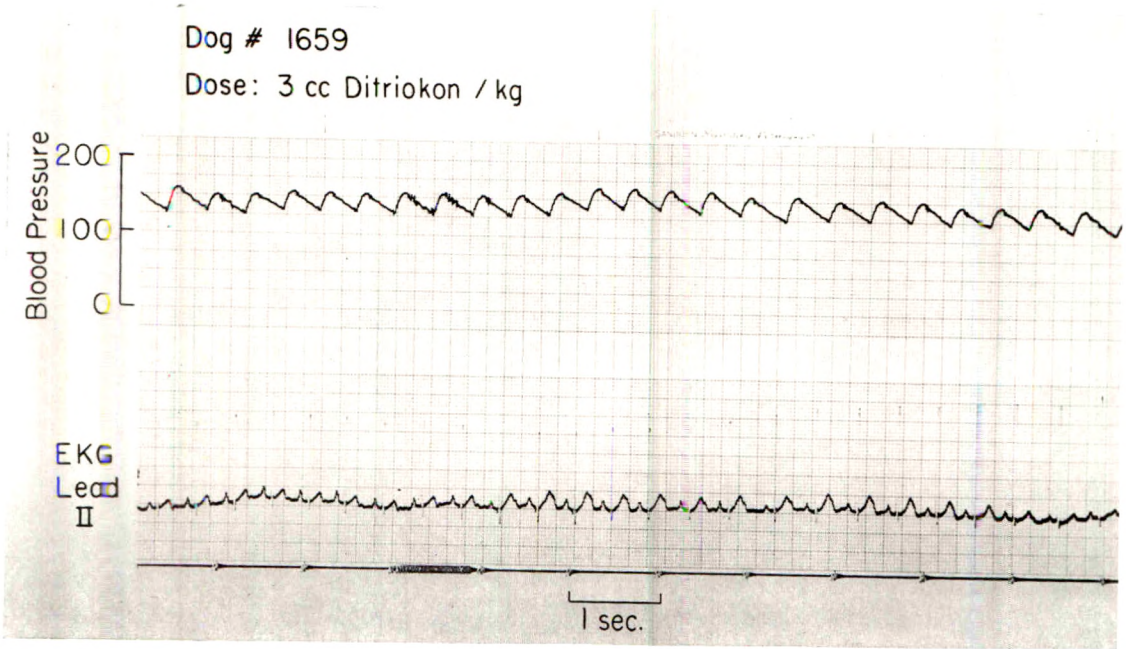


FIG. 2. Blood pressure and electrocardiographic response to the rapid intravenous injection of 3 cc./kg. ditriokon. Some ST segment and T wave changes are seen, along with a minor blood pressure depression. Injection is indicated on the timer tracing.

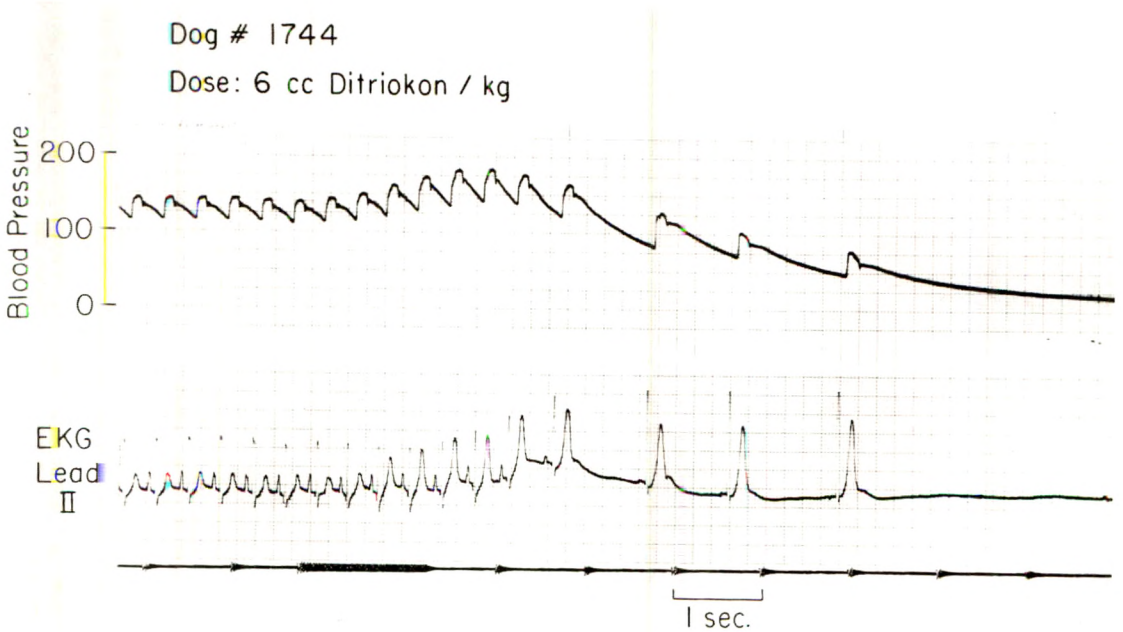


FIG. 3. Marked response to a 6 cc./kg. dose of ditriokon with some hypertension followed by profound hypotension and bradycardia. Note the almost immediate electrocardiographic changes, which begin within one second from the start of the injection (timer line).

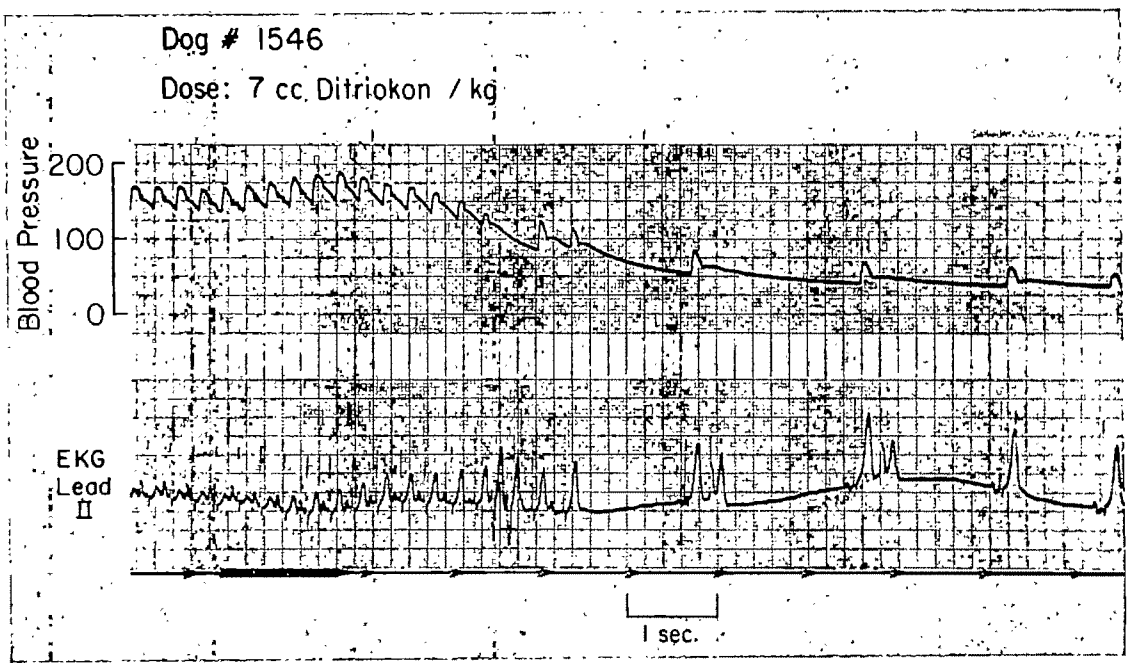


FIG. 4. An intravenous dose of 7 cc./kg. ditriokon was uniformly lethal. Marked electrocardiographic aberrations accompany the profound and rapidly fatal hypotension.

is essentially equal in osmolality to hypaque 90 per cent, and yet, utilizing identical injection procedures, it appears to have an LD_{50} approximately twice that of hypaque 90 per cent.[1] In this regard, it should be noted that the ditriokon injections were considerably more rapid than those of hypaque 90 per cent, as a result of its decreased viscosity, although the same injection apparatus was used in both studies. This factor was expected to increase its toxic effects, but despite this, the observed mortality was decreased.

B. VISCOSITY

Utilizing a modified Eckstein, Book and Gregg viscosimeter, measurements of the viscosity of a number of commonly utilized

TABLE II

OSMOLALITY AND IODINE CONTENT OF ANGIOGRAPHIC AGENTS

Preparation	Osmolality (mOsm./L.)	Per Cent Iodine (gm./100 cc.)	Ratio (osmolality/per cent I)
Renografin 60%	1360	29.3	46.5
Hypaque 50%	1376	30	45.9
Renografin 76%	1648	37	44.6
Hypaque 75%	1716	39.3	43.8
Cardiografin 85%	1900	40	47.5
Ditriokon 68.1%	1904	40	47.6
Hypaque 90%	2020	46	44.0
Urokon 70%	2140	46	46.5
Whole Blood	285	—	—
			Average: 45.8
			Range: 43.8–47.6

angiographic preparations were performed through a temperature range of approximately 0–50 C. The preparations studied included 50, 75 and 90 per cent hypaque,* 60 and 76 per cent renografin,† 85 per cent cardiografin† and ditriokon.

The results of these measurements are presented in Figure 5, in comparison with the viscosity of whole blood. It may be noted that ditriokon is considerably less viscous than the other tested agents with comparable iodine contents. In addition, it may be noted that heating this agent from room temperature (25°C.) to body temperature (37°C.) has little effect upon its viscosity, in contrast to the marked effects of heating some of the more concentrated diatrizoate preparations.

c. Comparative Injection Rates

Utilizing the information obtained from the viscosity measurements and the percentage of iodine contained in the various preparations, calculations of the comparative injection rates of (a) the volume of material and (b) the amount of iodine which can be injected with an identical injection pressure, catheter system, etc., have been made. For this purpose, the viscosity of the substances at room temperature has been utilized. It may be noted that more than 5 times as much ditriokon as hypaque 90 per cent could be injected in a given period of time, and this would contain 4.5 times as much iodine. These calculations assume laminar flow, which is a valid assumption only in low pressure injection systems. In high pressure injections, flow is often turbulent, and the differences between injection rates are not as marked as those calculated in Table III. In the acute animal toxicity studies, the ratio of the rates of injection of ditriokon and hypaque 90 per cent varied from 2 to 6.

Discussion

The animal toxicity studies indicate that massive doses of ditriokon may be given with considerably greater initial safety than equal doses of hypaque 90 per cent. The value of these observations for such studies as intravenous aortography appears obvious. While the clinical application of such large doses as have been used in these studies is not immediately justifiable, the utilization of ditriokon for such studies should be associated with increased patient safety, and some cautious increase in patient dosage may be justified.

The low viscosity of ditriokon permits

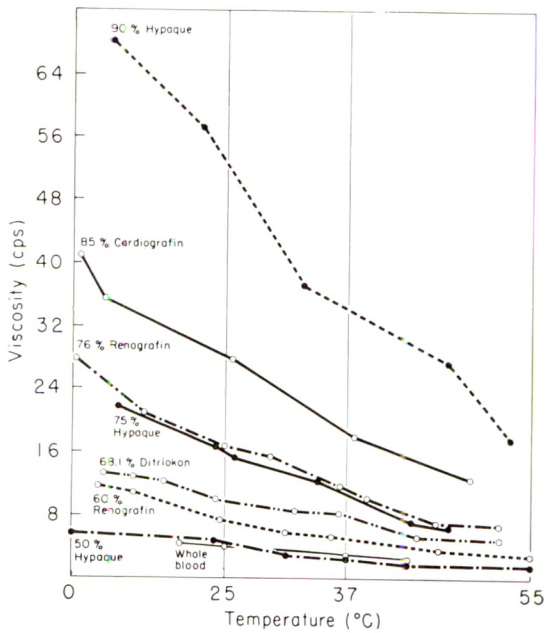


Fig. 5. Viscosity of commonly employed iodinated radiopaque compounds used for angiography over a temperature range from 0–50° C.

Table III

Calculated Comparative Injection Rates (per unit time)*

Preparation	Volume	Amount of Iodine
Hypaque 90%	1.0	1.0
Cardiografin 85%	1.8	1.6
Renografin 76%	3.1	2.5
Hypaque 75%	3.3	2.7
Ditriokon 68.1%	5.2	4.5

* Preparation at room temperature (25°C.), with standard injection pressure, catheter system, etc., and relative to hypaque 90 per cent as unity, based on viscosity measurements, and assuming laminar flow (see text).

* Generously supplied by Winthrop Laboratories, Inc.
† Generously supplied by E. R. Squibb & Sons.

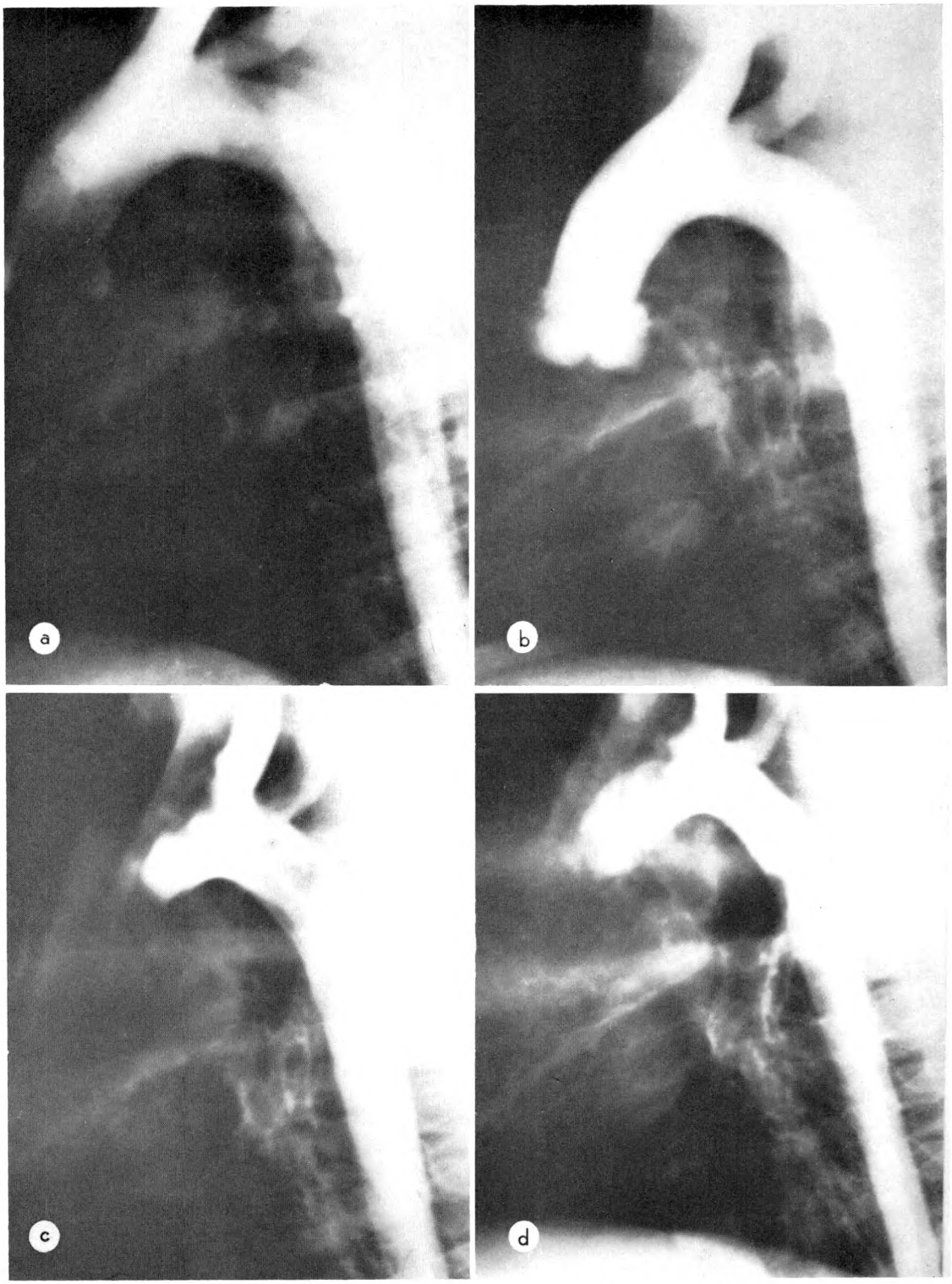


FIG. 6. Comparison of thoracic aortograms of the same dog, utilizing identical injection apparatus and pressure, and equal volumes of (*a*) hypaque 90 per cent, (*b*) ditriokon, (*c*) hypaque 75 per cent and (*d*) cardiografin 85 per cent.

its utilization at room temperature, as well as its more rapid injection under standard injection conditions. The marked decrease in cardiovascular reaction to this hypertonic agent, as compared with hypaque 90 per cent, is of considerable theoretic significance in any attempt to invoke hypertonicity alone as the cause of the hemodynamic alterations observed. The data presented appear to show that viscosity has a significant role in this mechanism.

While these studies indicate that ditriokon is relatively well-tolerated insofar as the acute cardiorespiratory response to rapid intravenous injection is concerned, it must be noted that the sodium diprotrizoate (miokon) fraction has been demonstrated to contain the potential for nephro-and neurotoxicity when administered separately. Long-term studies of the toxic potential of ditriokon to the kidney and the central nervous system therefore appear appropriate for future investigation.

SUMMARY

Experimental studies have been performed in an attempt to evaluate a new angiographic preparation. Acute intravenous toxicity studies in the dog indicate that the LD_{50} of ditriokon is approximately twice that of hypaque 90 per cent. The ratio of osmolality to percentage of iodine content is essentially constant for all the angiographic preparations studied. Viscosity studies indicate the capability of ditriokon to be delivered in large amounts per unit time (with high iodine content) under standard injection conditions. Ditriokon would appear worthy of clinical trial in procedures requiring large amounts of concentrated radiopaque angiographic media. Caution is advised, however, inasmuch as the potential of ditriokon to cause central nervous system and renal damage has not been evaluated in long-term experiments.

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THE ROENTGEN DIAGNOSIS OF HEMANGIOMA OF BONE*

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HEMANGIOMA of bone is a benign, slowly growing tumor arising from newly formed blood vessels and it is one of the primary osseous neoplasms. Histologically, two types are recognized, cavernous and capillary. The cavernous is made up of large, thin-walled vessels and sinuses which are lined by a single layer of endothelial cells interspersed among resorbed bony trabeculae. The capillary type is composed of fine capillary loops which tend to spread outward in a sunburst fashion. Cavernous hemangiomas are commonly found in the vertebrae and skull, while the capillary variety is more likely to be encountered in flat bones and in the metaphyses of the long bones.[50]

Osseous hemangiomas are rather rare tumors. The first report referring to the roentgen findings in this tumor was by Hitzrot[27] in 1917. Bucy and Capp[10] in 1930, described the appearances in 7 cases selected from the Bone Tumor Registry. Lichtenstein[39] has observed only a few of these neoplasms as surgical specimens. At the Mayo Clinic, Dahlin[17] encountered 13 hemangiomas of bone constituting 0.6 per cent of the total primary bone tumors at that institution. As Jaffe[30] has stated, when one excludes both the vertebral hemangiomas and those in the skull, then this type of primary neoplasm becomes an uncommon condition indeed.

A review of the material available to us brought to light 45 cases of primary hemangioma of bone, all of which were histologically proved except for a few having a characteristic roentgen pattern in the vertebrae and skull. The present purpose is to report the roentgen appearance of these tumors with the object of making their identification more reliable for the roentgenologist.

The location of the 45 hemangiomas is given in Table I.

TABLE I

LOCATION OF 45 HEMANGIOMAS

Spine				Facial Bones	
	Cervical	1		Mandible	3
	Thoracic	5		Nasal	1
	Lumbar	8		Zygoma	1
			Ribs		5
Skull		13	Clavicle		1
			Foot		2
			Long Bones		5

More than half of the hemangiomas were in the skull and spine. An inflated percentage of hemangioma in the other bones may be present because of the tendency of patients with tumors and tumor-like lesions of the bone to find their way to this institution plus the fact that a number of spinal tumors, having been discovered incidentally, undoubtedly escaped being recorded in the diagnostic files.

HEMANGIOMA OF THE SPINE

Because of a general familiarity on the part of radiologists with the appearance of hemangioma in this site, only a summary of the material will be given. Apparently there is a wide disparity between the anatomic and the roentgen incidence of vertebral hemangioma. This fact has been demonstrated by Schmorl,[52] Töpfer[58] and later by Junghanns.[35] In 3,829 vertebral columns studied in Schmorl's institute, the incidence of hemangioma was revealed to be 10.7 per cent, and another report of

* Presented at the Sixty-first Annual Meeting of the American Roentgen Ray Society, Atlantic City, New Jersey, September 27–30, 1960.

10,000 spinal columns studied revealed a similar incidence. It is now well known that the smaller, asymptomatic vertebral hemangiomas rarely can be demonstrated on roentgenograms, a fact proved by roentgen examination of autopsy material.

Hemangioma of the spine usually is a single lesion, but sometimes two or more vertebral bodies are involved. While the process is generally in the vertebral body, other portions of the vertebra can be the site of the disease. When the hemangioma is of adequate size, the roentgen diagnosis is usually not difficult.

There may be a slight general diminution in the over-all bone density of the vertebral body. The most characteristic finding, however, is the presence of parallel, somewhat fuzzy, vertical linear streaks, which give the so-called "corduroy cloth" appearance. This effect is noted particularly in the lateral projection, and it is sometimes accompanied, particularly in sagittal projection, by a fine reticulated or "honeycomb" texture. The cortex of the vertebral body may become somewhat fuzzy, ragged and ill-defined, but usually its outer border is intact (Fig. 1, *A* and *B;* and 2, *A* and *B*). With compression fracture, many of these characteristic findings become less evident or are obscured.

A compression fracture was observed in 3 instances. One, in which the compression of the body was only partial, showed that many of the roentgen characteristics of hemangioma were preserved (Fig. 3, *A* and *B*). In the second, the gradual progression of the compression was followed by serial roentgen studies (Fig. 4, *A*, *B* and *C*). The third revealed extensive destruction and such a pronounced degree of collapse of the vertebral body that roentgenologically a diagnosis of hemangioma could not possibly be made.

Most hemangiomas of the spine are asymptomatic. However, in 2 of the patients, there was a vague intermittent type of pain. In the 3 instances where compression fracture occurred, there were both subjective and objective findings. Two of the patients complained of severe pain in the back and examination disclosed spasm

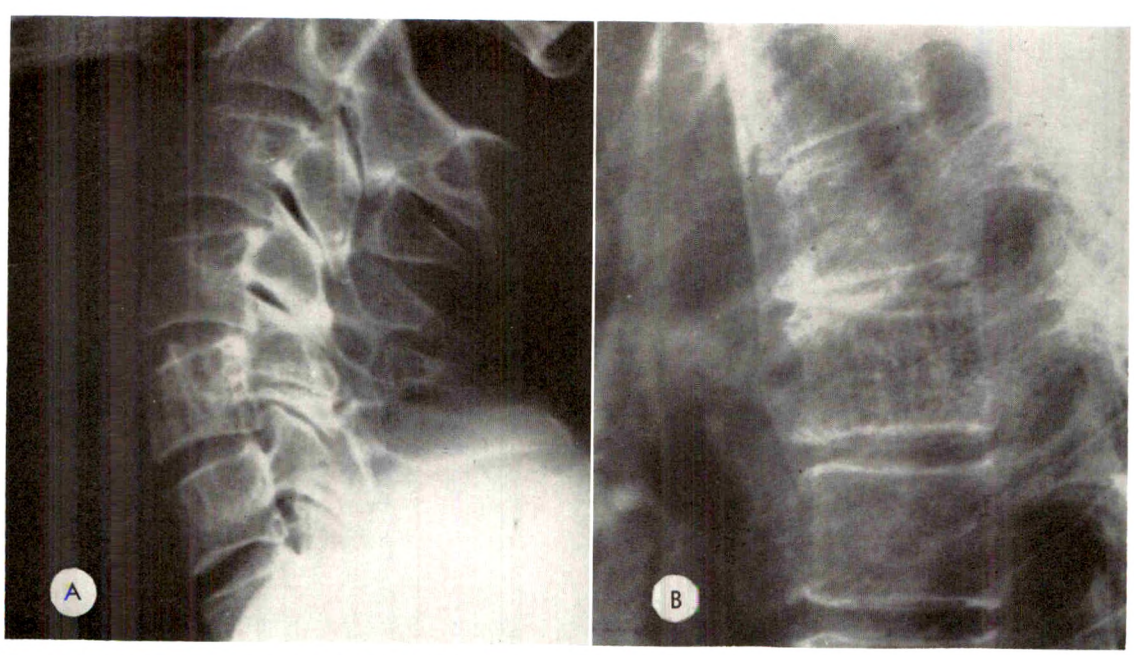


Fig. 1. (*A*) Hemangioma of the fifth cervical vertebra showing involvement of the body, pedicles and spinous process. (*B*) Hemangioma of the sixth thoracic vertebra. Note the pillar-like trabeculae running in a longitudinal axis.

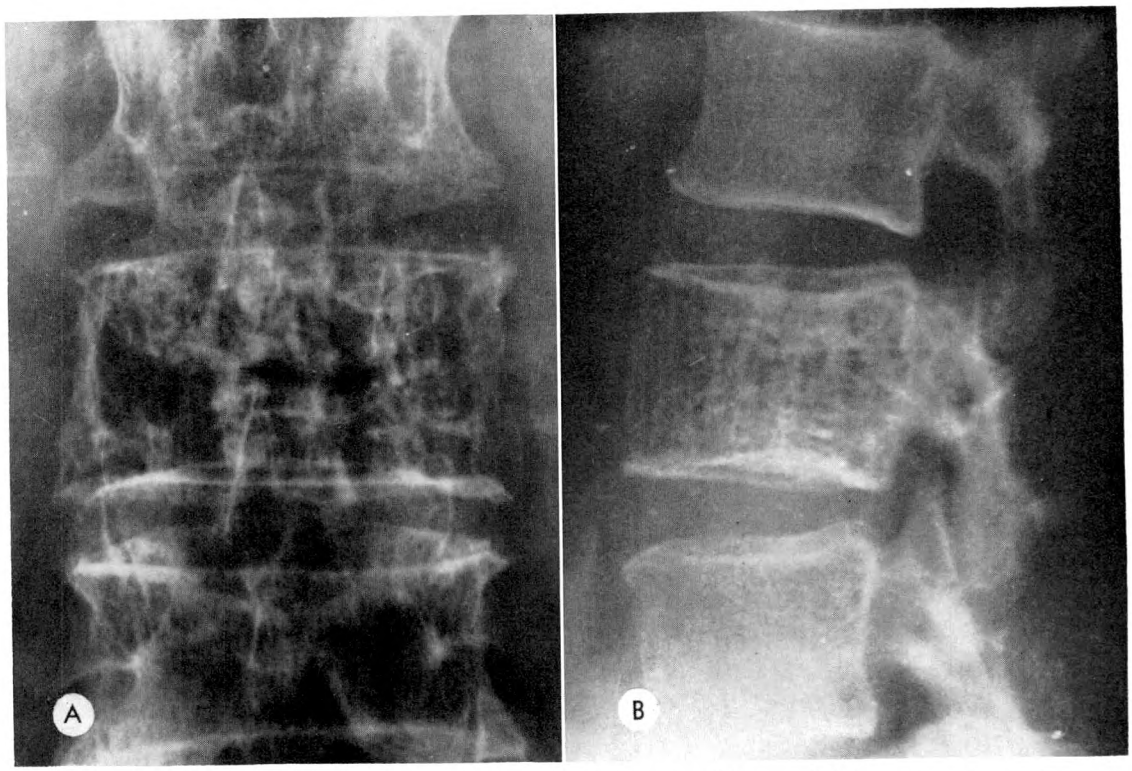


FIG. 2. (*A* and *B*) Hemangioma of the third lumbar vertebra. The parallel linear streaks running vertically in the body give a "corduroy cloth" appearance.

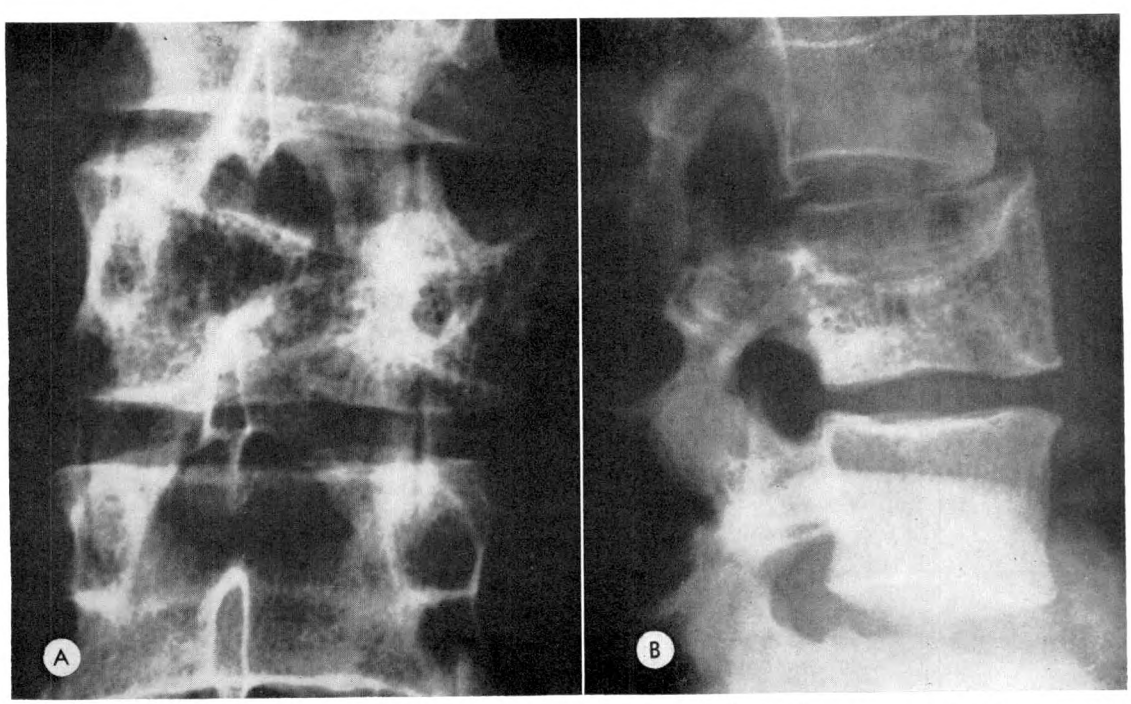


FIG. 3. (*A* and *B*) Hemangioma of the third lumbar vertebra complicated by a compression fracture. The characteristic vertical striations have been replaced by a coarse, irregular trabecular pattern.

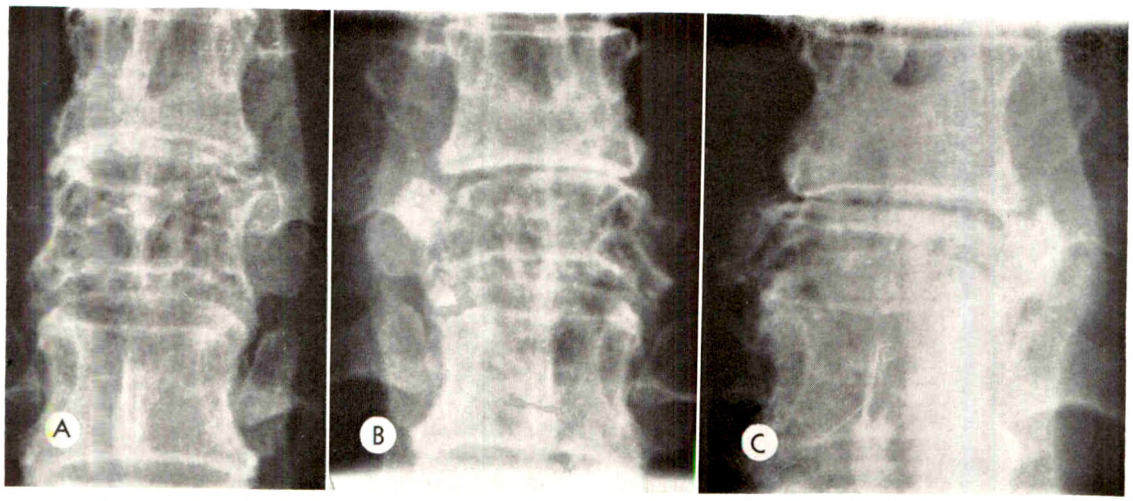


FIG. 4. (*A*, *B* and *C*) Hemangioma of the ninth thoracic vertebra showing interval compression over a period of ten weeks.

and rigidity of the muscles of the lumbar region. The third displayed signs of compression of the spinal cord as evidenced by spastic paraplegia with a sensory level at the thoracic segment. Four of the patients were treated by irradiation and showed a satisfactory response. Two were relieved of their complaints, and they have remained symptom-free for more than ten years.

Schlezinger and Ungar[51] reviewed the literature in 1939 and added 2 cases of their own to make a total of 40 patients who had neurologic changes associated with compression of the spinal cord due to hemangioma of bone. Robbins and Fountain[49] recently reported a successfully treated case of hemangioma of the cervical vertebrae with severe myelocompression, stating that it was the eleventh such case described.

In the differential diagnosis, hemangioma of the vertebrae sometimes must be distinguished from Paget's disease. In osteitis deformans there is usually a more uniform increase in bone density and there is framing of the vertebral body by a zone of cortical thickening and sclerosis. Malignant lymphomas occasionally show changes similar to hemangioma of bone and metastatic cancer and multiple myeloma similarly must be considered in differential diagnosis.

HEMANGIOMA OF THE SKULL

The first such case was reported by Toynbee in 1845. In 1949, Wyke[60] reviewed the literature and uncovered 39 primary angiomatous lesions in the skull.

The hemangiomas of the skull reported here are confined to the frontal bone. The lesion tends to be quite typical roentgenologically, being represented by a single area of rarefaction, which is usually either round or oval in shape. There is a variation in size from 1 to 7 cm. in diameter. The internal pattern is characterized by fine, delicate striae or reticulations, which being closely knit often assume a "honeycomb" appearance (Fig. 5, *A* and *B;* and 6). These striations on occasion are exaggerated and give a "sunburst" appearance.

A few of the smaller lesions seemed almost entirely lytic with no discernible internal pattern. The margins of the defects were sharp and well delineated from the surrounding normal bone and sometimes a fine margin of bone condensation was seen at the periphery.

Several cases were somewhat atypical. One was spindle-shaped, measuring 7.0×2.5 cm. Another of the larger lesions, measuring 5.5×5.0 cm., showed a centrally placed radiolucency surrounded by the usual

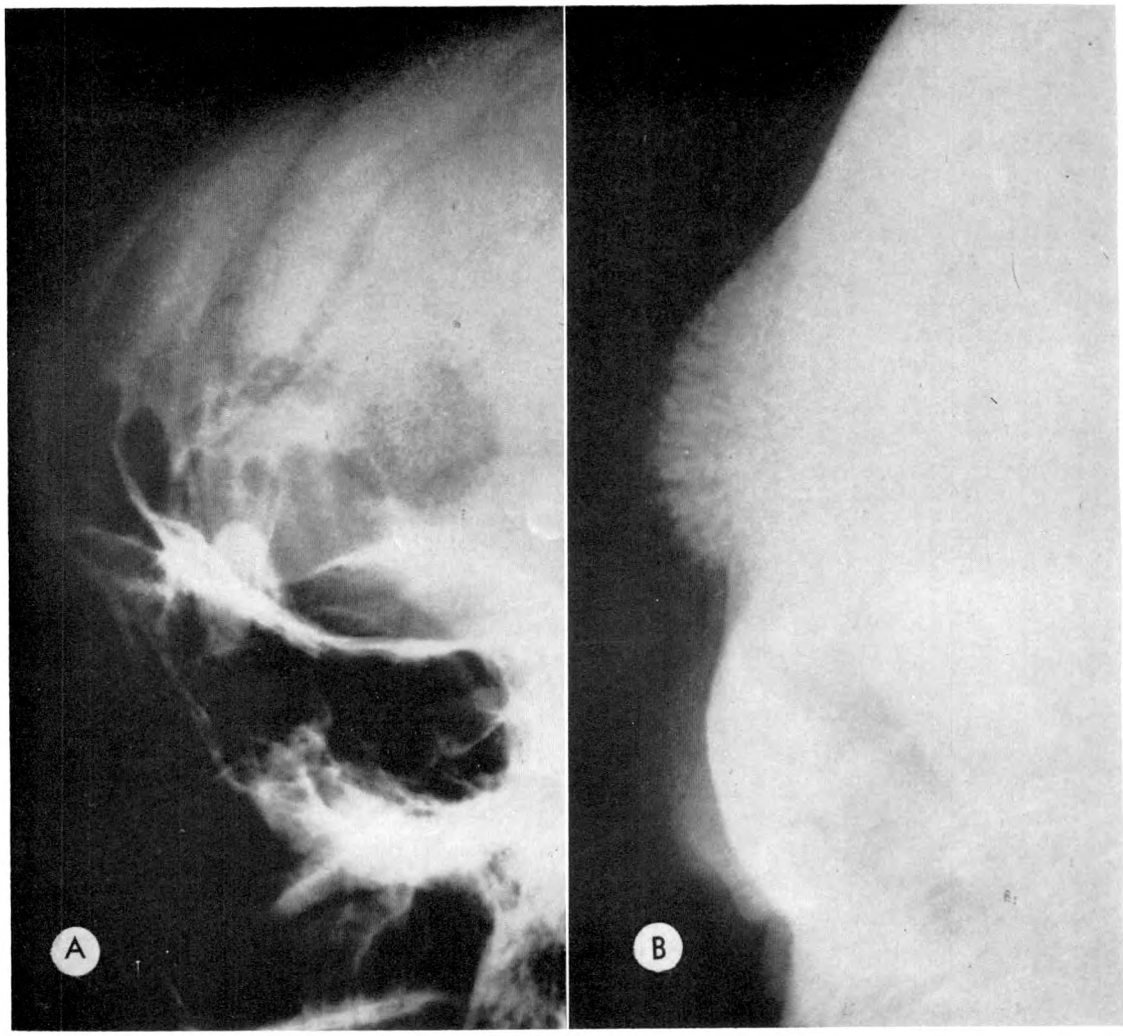


FIG. 5. Hemangioma of the skull. (*A*) A round area in the frontal bone showing a finely porous "honeycomb" rarefaction. (*B*) Tangential view of same skull showing radial striations giving the "sunray" type of appearance.

"honeycomb" type of septation, while at the periphery of the lesion there were clustered small, round, fairly distinct radiolucent areas. A hemangioma measuring 3×3 cm. and seen as a round defect in the right frontal bone had a dense compact segment of bone in its medial portion. However, there was an accompanying "honeycomb" pattern surrounding the dense central area. One hemangioma was purely lytic in one half of the lesion, whereas the other half presented the characteristic "honeycomb" reticulation.

Tangential or profile views are particularly informative and constitute a necessary part of the roentgen examination of lesions in this area. Ordinarily, the bony tumefaction is seen extending outwards beyond the normal confines of the bone. This external bulging is sometimes accompanied by an erosion of the outer table of the skull, whereas the inner table tends to be well maintained. The profile view frequently discloses vertical striations assuming a "sunray" type of appearance. These bony striae seem to be directed in a radial

manner as though originating from a common center (Fig. 5*B*). Six of the cases presented this appearance.

Conditions to be considered in differential diagnosis include cancer metastases and multiple myeloma, and, when the profile views reveal vertical striations, a meningioma may have to be ruled out. A few hemangiomas bear a close resemblance to epidermoids. However, the outline of these lesions tends to be more serpiginous, the margins are fairly dense due to a fine sclerotic border, and they do not have a reticulated or "honeycomb" pattern. Osteoma at times closely resembles hemangioma and in some instances the differential diagnosis is almost impossible to make with assurance. Generally speaking, however, an osteoma is uniformly dense or has a pattern that looks more like normal trabeculae.

HEMANGIOMA OF THE MANDIBLE

Two of the 3 cases in the mandible presented a fairly classic roentgen appearance. One was a nineteen year old female who had noted a swelling two years previously. This gradually increased in size.

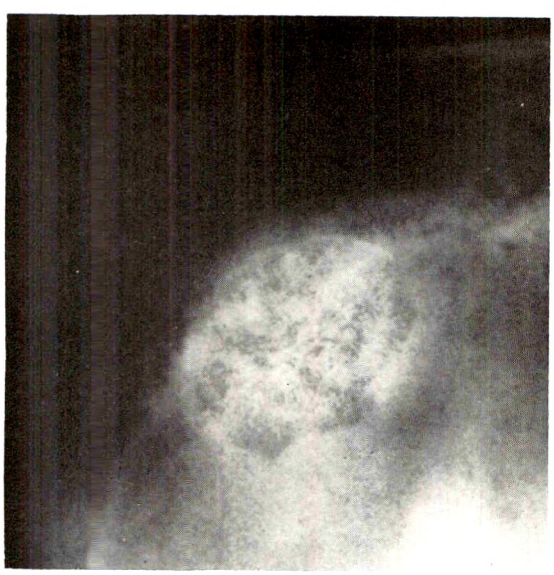


Fig. 6. Hemangioma of the skull showing a more coarse "honeycomb" rarefaction.

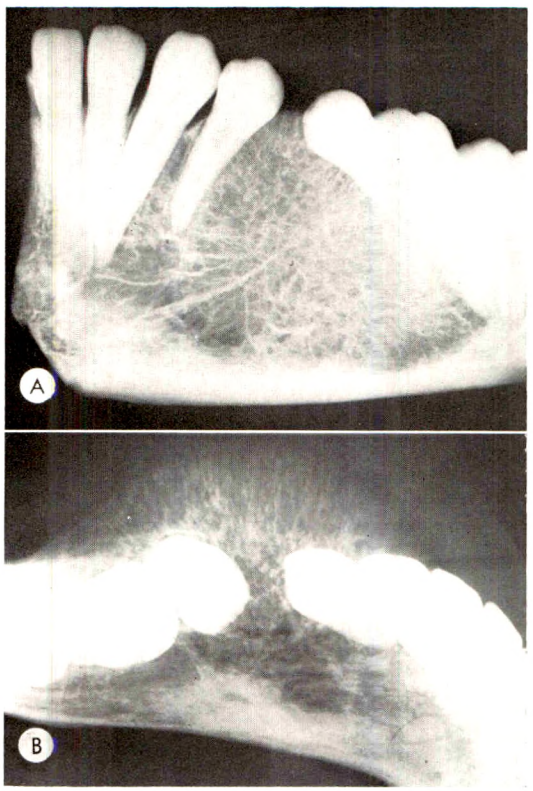


Fig. 7. Hemangioma of the body of the mandible. (*A*) A roentgenogram of the gross specimen showing the classic "sunray" appearance. (*B*) Tangential view showing the characteristic radiating spicules at right angles to the bone.

Physical examination showed a hard enlargement, 4×3 cm., which involved the entire thickness of the bone. Roentgen examination demonstrated a multiloculated expanding lesion in the body of the left side of the mandible. The expanded area contained thick coarse trabeculations radiating outwards from a somewhat ill-defined center point. The cortex was intact and there was no evidence of any soft tissue component. The pathologic diagnosis from an incisional biopsy was hemangioma of bone, cavernous type.

A roentgenogram of the second case revealed an expanding, osteolytic lesion with numerous trabeculae radiating in all directions. Tangential views displayed characteristic radiating spicules at right angles to the surface of the bone. A roentgenogram

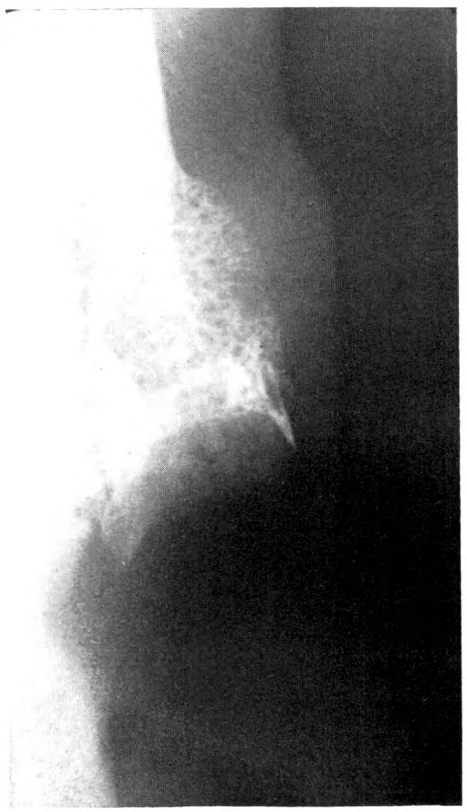


FIG. 8. Hemangioma of the nasal bones. The internal pattern of the expanding lytic lesion is that of a fine fibrillary network of bony striae.

of the resected gross specimen showed the classic "sunray" appearance (Fig. 7, *A* and *B*).

Castleman[12] discussed a case of hemangioma in the mandible from the files of the Massachusetts General Hospital, in which the roentgenograms showed an expansion of the bone, thinning of the cortex and an irregular, fine lacy osseous network producing honeycombing.

HEMANGIOMA OF THE NASAL BONES

The first case of primary hemangioma of the nasal bones was reported in 1936 by Neivert and Bilchick.[42] Another was described by Bloom[3] in 1954. The roentgenograms of the presently reported case showed an expanding predominantly lytic lesion, ovoid in configuration. The cortex was completely gone, but there did appear to be a fine limiting shell of periosteal new bone. The internal pattern of the tumor created a fine fibrillary network, highly suggestive of the diagnosis of hemangioma (Fig. 8).

HEMANGIOMA OF THE ZYGOMA

This is the only case known in which hemangioma has been described in this bone.

The patient, a forty-six year old female, noted a swelling below the left eye for two years. Physical examination disclosed a bony protrusion 2.5 cm. in diameter along the inferior outer portion of the left orbit.

Roentgenographic examination demonstrated a somewhat expanding lytic lesion in the superior portion of the left zygoma. The inferior margin of the lesion was distinct and the internal pattern of the tu-

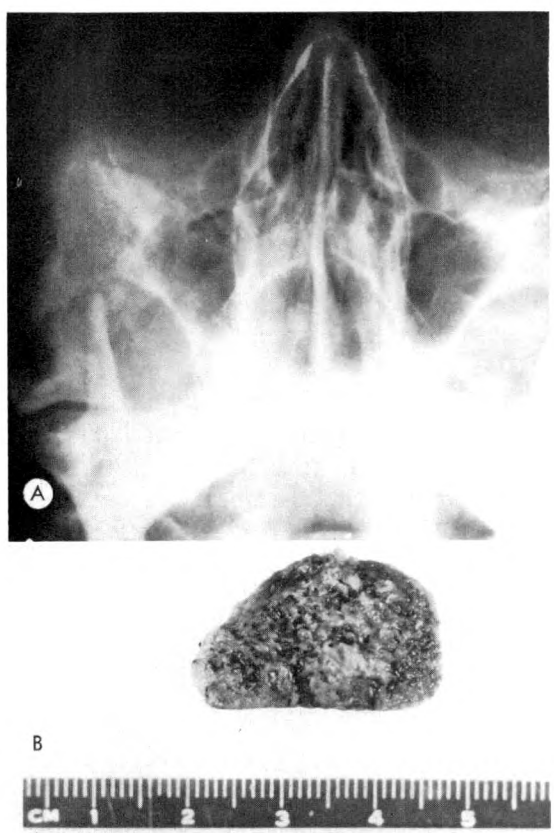


FIG. 9. Hemangioma of the right zygoma. (*A*) The interior of the tumor shows an exaggeration of the diploic spaces giving a "honeycomb" type of appearance. (*B*) Photograph of resected specimen.

mor had a reticulated and "honeycomb" appearance (Fig. 9, *A* and *B*). In general the roentgen appearance of the lesion was quite typical. The tumor was completely excised. The pathologic diagnosis was hemangioma of bone.

HEMANGIOMA OF THE RIBS AND CLAVICLE

The roentgen appearance of hemangiomas in these sites was sufficiently unique so as to offer special problems in differential diagnosis.

A thirteen year old white male with a rib lesion was struck in the right side of the chest two years previously, suffering sufficient pain to require strapping. Since that time, there had been intermittent discomfort. Physical examination disclosed tenderness, but no swelling.

Roentgen examination showed an expanding lytic lesion anteriorly in the right sixth rib. The bony architecture was completely lost in a portion of the defect. A very faint cortical rim could be detected about the periphery, forming a sharp line of demarcation with the normal bone. The rib was resected and the pathologic diagnosis was hemangioma. The roentgen appearance of this tumor can hardly be considered typical of hemangioma. Some resemblance to giant cell tumor, fibrous dysplasia and chondroma is noticeable.

A routine chest roentgenogram revealed a puzzling process in the left fifth rib of a twenty-nine year old female who was asymptomatic. The posterior portion of the rib was widened and replaced by a coarse web-like pattern of vacuolated appearance. The superior and inferior borders formed irregular, thinned-out cortical margins, and there were a few bony septa or ridges perpendicular to the axis of the rib. A surrounding soft tissue mass measuring about 6 cm. was present (Fig. 10, *A* and *B*). A resection of the fourth, fifth, sixth and seventh ribs was carried out and the histologic diagnosis was hemangioma of the bone. The roentgen appearance of this particular tumor can be confused with osteogenic sarcoma because of the irregular destruction of bone, the unusual internal pattern and the soft tissue mass. The significant point here is the fact that a soft tissue mass may occasionally accompany hemangioma of bone.

On a routine chest roentgenogram of a thirty-five year old asymptomatic female, a bizarre expanding defect of the right eighth rib was discovered. This portion of

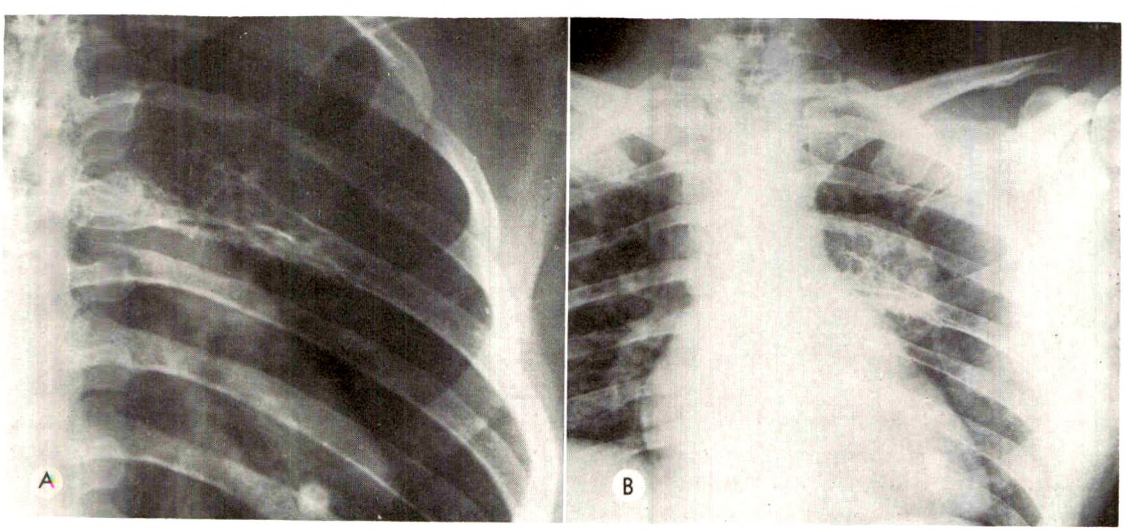


Fig. 10. Hemangioma of the left fifth rib. (*A*) The posterior portion of the rib is widened and replaced by coarse bony septa which give the bone a vacuolated appearance. (*B*) A chest roentgenogram showing a soft tissue mass surrounding the rib lesion.

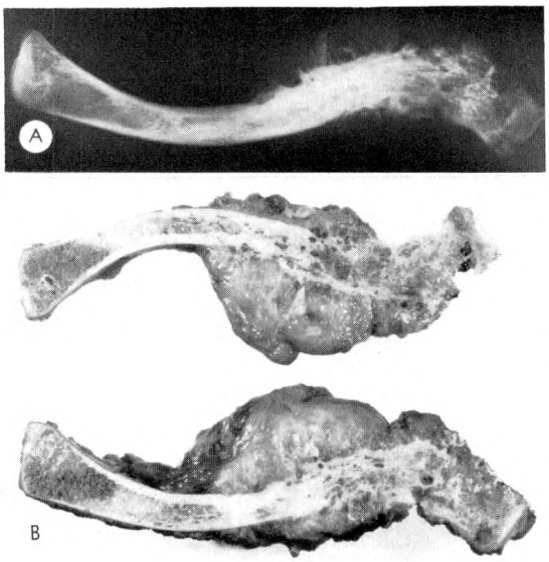


Fig. 11. Hemangioma of the clavicle. (*A*) roentgenogram of the gross specimen showing an exaggeration of the diploic spaces giving the bone a coarsely porous "honeycomb" pattern. The cortex is gone and perpendicular spiculations can be seen along the upper and lower borders of the external end of the clavicle. (*B*) A photograph of the gross specimen showing a lobulated soft tissue angiomatous mass surrounding the bone tumor.

the rib was enlarged to about twice its normal diameter and it presented a multiloculated appearance. Lytic areas were surrounded by irregular formations of bone. Cortical margins were thinned-out and distorted, and some areas appeared to be destroyed, particularly along the inferior border. The right eighth rib was resected and the pathologic diagnosis was cavernous hemangioma.

Again a diagnosis of malignant tumor, particularly osteogenic sarcoma, would have to be considered although the fairly well formed locules, the quite sharp line of demarcation between the involved and the normal bone, and the absence of periosteal reaction would be points of some value against malignant tumor. Castleman[11] discussed a very similar case and stated that it was the only one he had ever seen in a rib.

A forty-four year old white male stated that a lump had been present on his left collar bone for about nine years, following an injury. There was some associated pain which had increased in time. Roentgen therapy was given with some relief of symptoms. Recent physical examination disclosed a fixed, nontender mass in the outer third of the clavicle, which measured 5 cm. in diameter (Fig. 11, *A* and *B*).

This particular case is unusual not only because of the clinical history but the fact that the roentgen appearance strongly suggested a malignant tumor, especially osteogenic sarcoma, except that the bone destruction in the spongiosa was quite orderly and the existing "honeycomb" pattern would not ordinarily be encountered in a malignant neoplasm.

Bucy and Capp[10] reported a somewhat similar appearing tumor at the sternal end of the clavicle.

HEMANGIOMA OF THE BONES OF THE FOOT

One of the 2 cases of tumors occurring in this area is of special interest.

The patient was a fifty-five year old white female who had fallen and injured her right foot fifteen years previously. Eight weeks after the injury she complained of pain and some swelling was then noted. The pain subsided, but the swelling persisted for about ten years or so, after which she thought that an increase in the size of the swelling had taken place. Physical examination revealed a bony hard mass on the dorsum of the foot.

Roentgen examination showed a somewhat rarefied expanding lesion involving the entire extent of the first metatarsal and the adjacent tarsal bones of the foot as well. There were innumerable small locules giving the involved bone a characteristic "soap-bubble" appearance. A tangential view showed numerous fine delicate septa tending to run perpendicular to the long axis of the metatarsal bone (Fig. 12). The lesion was removed and the pathologic diagnosis was hemangioma of bone.

HEMANGIOMA OF SOFT PARTS INVADING BONE

Twenty-three cases were studied roentgenologically in which patients with soft tissue hemangiomas were subjected to roentgen examination. In 15 of these there was roentgen evidence of bone involvement. In most instances the hemangioma of the soft parts harbored multiple, round discrete calcifications representing phleboliths, a finding not noted in primary hemangioma of bone.

Soft tissue hemangiomas may reach very large proportions without involving bone, but if the neighboring bone is affected, it it may be altered in various ways. The simplest type of secondary change is merely a smooth indentation or erosion of the cortex. This was noted in 3 of the 15 cases. Another group showed a triad of roentgen findings; *viz.*, enlargement of the bone, coarsening of the bony trabecular structure and thinning of the cortex. In other instances pressure-type deformities of the neighboring bones were encountered. There was one such instance in which the tibia and fibula showed a saucerized defect with anterior bowing secondary to the presence of a large hemangioma (Fig. 13). In addition, the bony texture was altered to a degree that suggested the presence of hemangioma within the bone itself.



Fig. 12. Hemangioma of the first metatarsal and adjacent tarsal bones of the foot. The presence of numerous small locules give the bone tumor a "soap-bubble" appearance. Note the numerous fine delicate septa running perpendicular to the long axis of the bone.

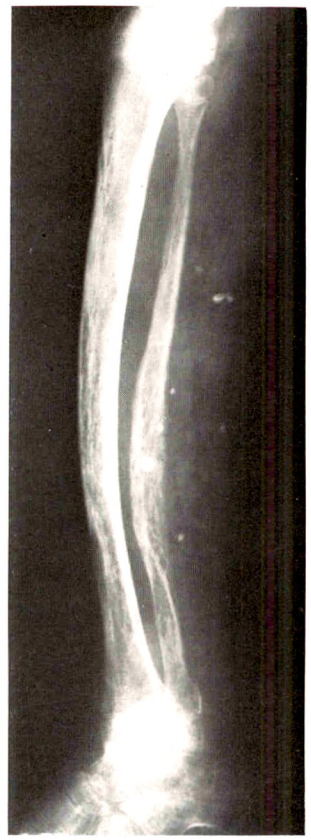


Fig. 13. Pressure deformities of the tibia and fibula. The trabecular structure is unusually coarse because of widening of the diploic spaces. Note the presence of phleboliths in the surrounding soft tissue tumor.

HEMANGIOMATOSIS

Multiple hemangiomas may develop independently throughout the body. Two of the patients examined showed diffuse involvement of the arm and forearm. Four displayed extensive disease of the thigh and leg. One revealed widespread hemangiomatosis of the toes, while another presented multiple soft tissue hemangiomas in both hands and both legs. The soft tissue changes were often accompanied by definite enlargement of the neighboring skeletal parts (Fig. 14, *A* and *B*).

One of the more striking examples of hemangiomatosis was a case of a sixty-five year old female who had had numerous blood vessel tumors since the age of three.

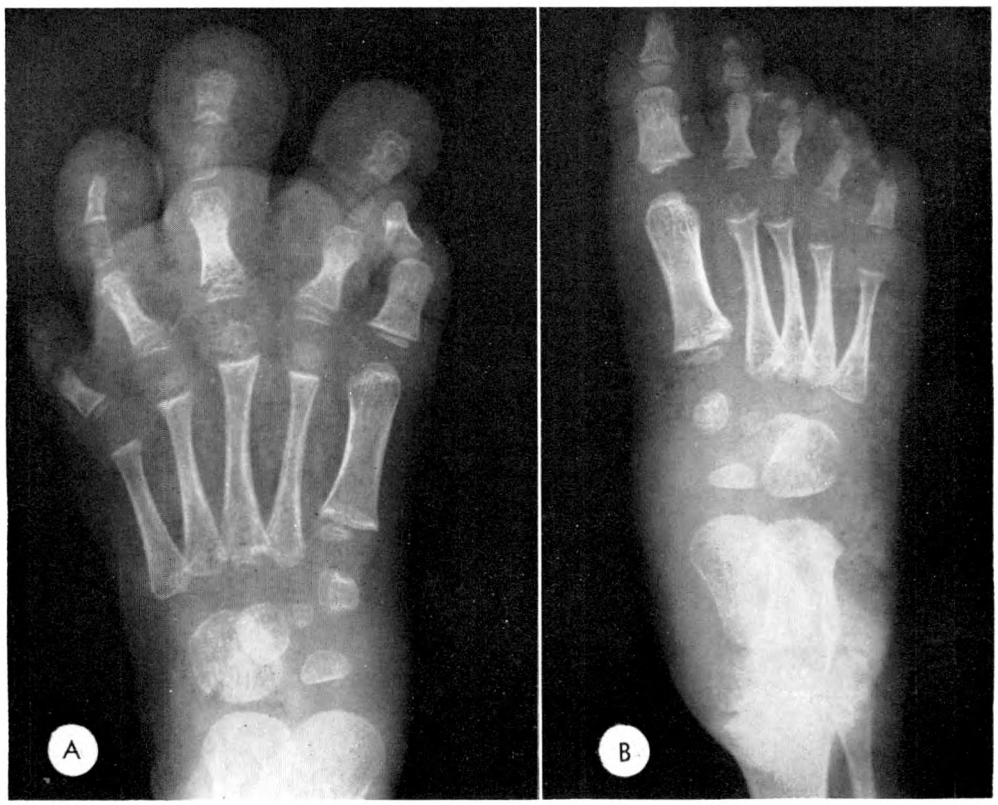


FIG. 14. Soft tissue hemangiomas producing secondary changes in bones. (*A*) Widening of the phalanges of the left foot. (*B*) The normal right foot is shown for comparison.

Many of these were removed when the patient was fourteen years old and others were excised ten years later. The lesions subsequently recurred and increased in size so that they were visible over the entire body with the exception of the right upper extremity, the lower half of the left leg and the left foot. In the neck and abdominal wall in particular, numerous subcutaneous, soft, bluish-red, nonpulsating vascular lesions were encountered.

Roentgen examination showed that both lower extremities were diffusely involved by soft tissue hemangiomas. The large nodular soft tissue masses could be seen projecting from the skin surface and similar nodules could be detected in the deeper soft parts as well. There were many phleboliths. Pronounced changes were noted in the feet; there was disappearance of the phalanges of a number of toes and the metatarsals were attenuated and spindle shaped (Fig. 15 *B*). There was cortical thickening in many of the long bones with peculiar wavy irregularities in marginal outline. Ill-defined bony overgrowths projected from the shaft in a perpendicular fashion and there seemed to be actual sequestration of bone in some areas. Somewhat similar, although less severe, changes were noted in some of the bones of the upper extremities. Many of the phalanges of the hands showed fairly typical angiomatous changes without accompanying soft tissue hemangioma in the immediate vicinity (Fig. 15 *A*). Although the patient is currently under treatment, the prognosis is poor due to the presence of chronic nephritis and hypertension.

A similar case was reported by Bonse.[9] His patient was a seventeen year old girl who showed numerous soft tissue tumors in the region of the right supraclavicular fossa and over the right hemithorax, right arm and back.

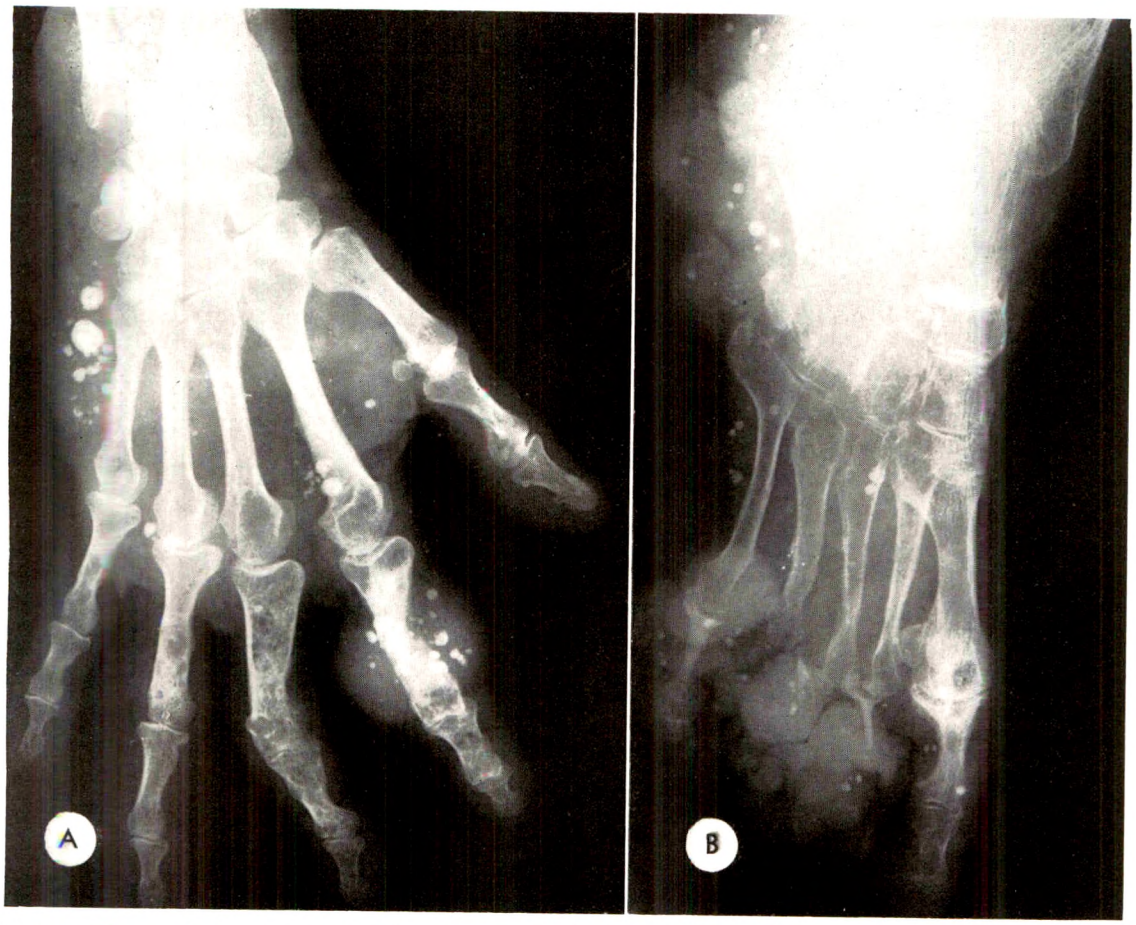


Fig. 15. Hemangiomatosis. (*A*) Multiple, fusiform, soft tissue hemangiomas of the left hand with cyst-like expansion of the phalanges and pressure deformities on the phalanges and metacarpals. (*B*) Nodular soft tissue tumors of the feet with a disappearance of the phalanges of four toes. Note the attenuated and spindle-shaped metatarsals. There were similar, widespread changes noted throughout the body.

SUMMARY

1. The spine and skull are the most frequent sites for the occurrence of primary hemangioma in bone and the roentgen features are usually characteristic. The "corduroy cloth" appearance prevails in the spine and the fine "honeycomb" pattern in the skull.

2. In the flat bones, the "sunburst" and "honeycomb" patterns are fairly regularly encountered, but the roentgen diagnosis is not always easy.

3. In other skeletal sites, it is not unusual to see a "soap-bubble" appearance and this is often combined with a "honeycomb" pattern.

4. In some instances, particularly in the ribs and clavicle, a hemangioma of bone may present findings closely resembling a malignant bone tumor such as an osteogenic sarcoma.

5. Soft tissue hemangioma as well as hemangiomatosis may involve the bone secondarily causing local deformities, enlargement, cortical thinning, and altered texture.

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RESPONSE OF FILM-SCREEN COMBINATIONS TO VARIATION IN ROENTGEN-RAY KVP.

By JACOB KASTNER, W. C. McLAUGHLIN, W. G. CIBULA, *and* J. A. MACKIN
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THERE has been increasing interest in the use of higher and higher kilovoltages for diagnostic roentgenography.

Over a long period of time and in the course of other work, we have gathered data on the response of different film-screen combinations to variations in roentgen-ray kilovoltages. This information is presented, along with the general procedure which was employed, in the hope that the results may be of practical interest to the radiologist in his choice of film-screen combinations and kvp. It is, of course, to be understood that this work ignores completely such problems as contrast and detail, which affect the reading of roentgenograms.

GENERAL PROCEDURE

In all cases a determination was made of the relative mas. required to produce a diffuse film density of unity.

Data for kilovoltages below 140 kvp. were obtained using both self-rectified and constant potential roentgen-ray equipment and a water phantom. A 280 kvp. Vanguard roentgen-ray unit was employed with a water phantom to obtain data for kilovoltages above 100 kvp. An overlap was thus provided for verification of the validity of our procedure and results at the higher kilovoltages.

Incident exposure dose measurements were made using standard self-reading pocket dosimeters, the energy and dose-rate response of which were well within the limits of these experimental conditions. The measurements were sufficiently well replicated to provide good confidence limits and excellent reproducibility was obtained over a period of years and a variety of conditions.

RESULTS AND OBSERVATIONS

The commercial film-screen combinations were examined for their response to the different peak kilovoltages. Representative results of the measurements for the most common combinations are shown in Figures 1 and 3. The relation of incident air dose rate to peak potential given in Figure 2 was used to develop the relation in Figure 3. Note the reverse trend beyond 200 kvp. It should be remembered that the skin dose, which includes backscatter, is also a function of kvp. A curve of the skin dose will have its minimum shifted slightly towards a higher kvp.

Table 1 presents the relative mas. required to produce the same film density at 180 kvp. for different commercial film-screen combinations. This kvp. was chosen

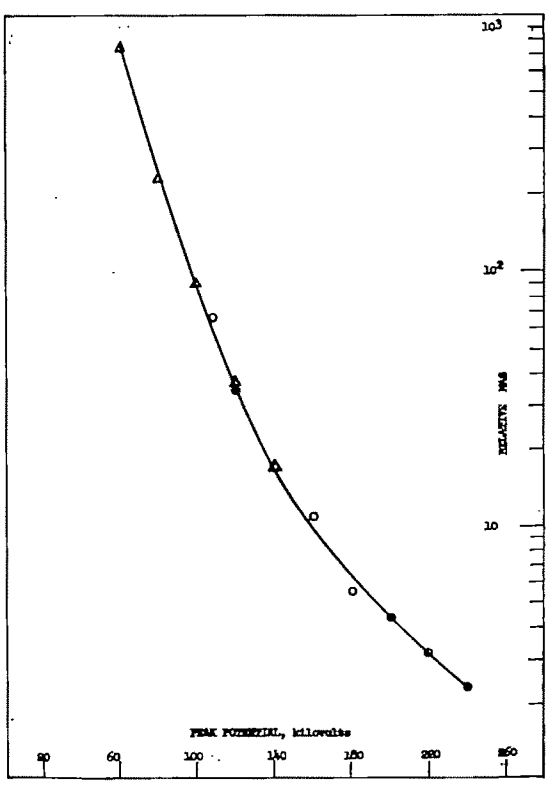


FIG. 1. Peak potential *vs.* relative mas. required to produce a diffuse density of 1.0 on standard film-screen combinations. ⊙—high potential roentgen-ray unit; △—low potential roentgen-ray unit.

TABLE I

RELATIVE mas. AT 180 kvp. FOR SOME FILM-SCREEN COMBINATIONS

Film	Screen	mas.
Kodak Blue Brand	du Pont Par Speed	6
Kodak Blue Brand	Ilford Standard	6
Kodak Blue Brand	Radelin General Purpose	6
Kodak Blue Brand	Ilford High Definition	13.5
Kodak Blue Brand	Radelin High Speed	2.5
Kodak Blue Brand	Radelin High Resolution	19
Kodak Blue Brand	Radelin Ultra Detail	22
Ansco High Speed	du Pont Par Speed	5
du Pont 508	du Pont Par Speed	7
Ilford Red Seal	du Pont Par Speed	6
Kodak Royal Blue	du Pont Par Speed	5

merely because this is probably as high a kilovoltage as anyone is likely to use. The relationship with kvp. for all combinations

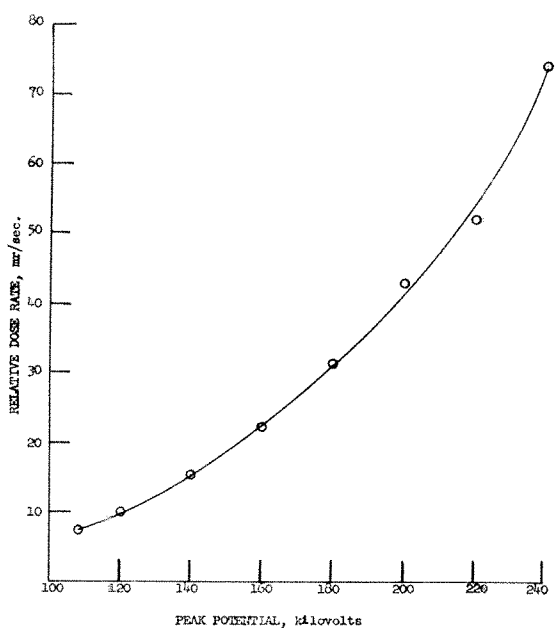


FIG. 2. Relative air dose rate *vs.* peak potential.

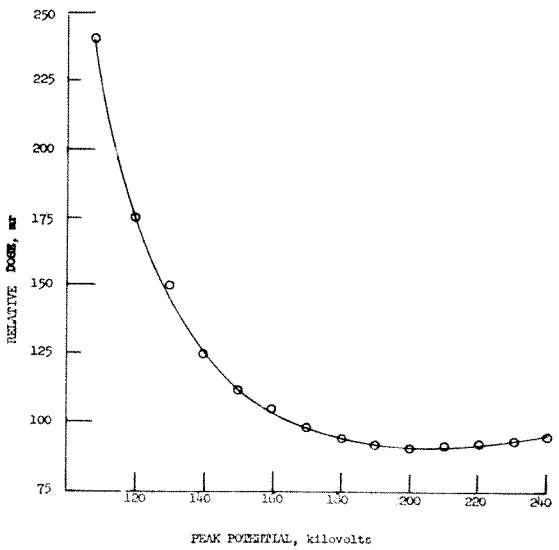


FIG. 3. Relative incident air dose *vs.* peak potential to produce a diffuse density of 1.0 on standard film-screen combinations.

except the Ilford H. V. screen is parallel to that of the common combinations shown in Figure 1. Our observations indicate that there is usually a relatively greater dose reduction obtained from the combination of a "high speed" screen with a standard film than from the converse, *i.e.*, a standard screen and a "high speed" film. This is in substantial agreement with data reported in 1948 by Van Allen.[1]

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We are indebted to Mr. Frank Dreisinger, Director of Medical X-Ray Education, for pointing up the medical interest in this problem.

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AN IMPROVED PATIENT HANDLING DEVICE*

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HOSPITAL patients often are not only unable to stand, but even unable to move from a litter to a roentgenographic table. There is a need, therefore, for a device to assist technicians in moving these patients. Such a device should offer the following features: (1) for the patient it should be safe and should necessitate practically no exertion; (2) for the nurses and technicians who use the device, it should require the exertion of so little physical strength that it is easy for even an unassisted woman to use; and (3) for the hospital which pays for the device, it should be inexpensive and capable of being made in the maintenance shop. A device meeting these specifications has been developed. It was found, incidentally, that it allowed special roentgenographic projections not otherwise easily obtainable.

Figure 1 is a photograph of the device when not in use. A Hoyer lift,* which consists of a boom elevated by a hand operated hydraulic cylinder mounted on casters, was modified. The U-shaped base was widened in the hospital maintenance shop so that it would straddle the pedestal of the x-ray machines. A horizontal plate was then welded to the end of the boom. Chains with hooks at each end connected this plate with the U-shaped cradling device shown. The arms are about 19½ inches wide and 10½ inches apart.

Figure 2 shows two rods inserted in a canvas stretcher and engaged by the lift. A patient is seen suspended in the lift and positioned for a lateral chest roentgenogram using the table Bucky diaphragm. The suspension arrangement shown prevents the patient from swinging and reduces the need to change his position in order to balance the stretcher in the horizontal position.

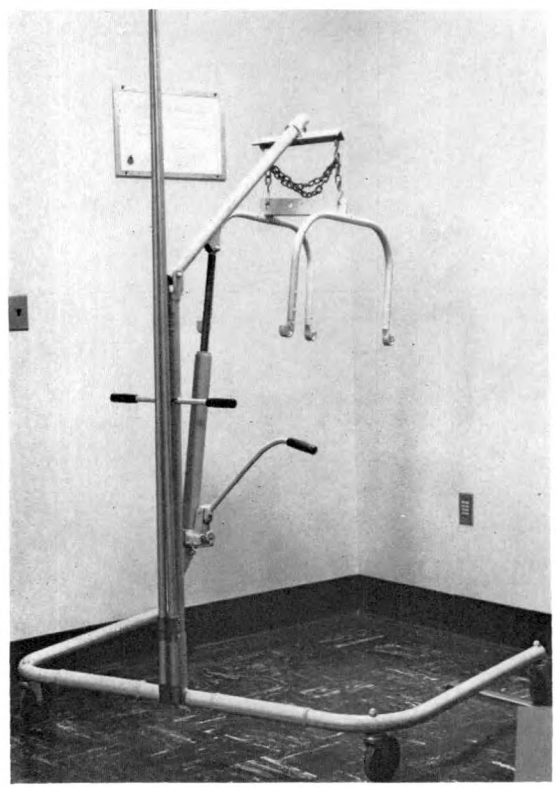


FIG. 1. The appearance of the device when not in use.

The canvas stretcher is the key feature of this device. It is obvious that, once the patient is on the canvas, the lift can be easily engaged and the patient can be moved anywhere in the hospital without further effort. Since the canvas is radiolucent, roentgenography and fluoroscopy can be done through it without interference. The long bars in the stretcher lie to the sides, well out of the roentgen-ray field. Initially, the canvas can be worked under a patient by rolling him from side to side

* Manufactured by Ted Hoyer and Company, Oshkosh, Wisconsin.

* From the Department of Radiology, Lemuel Shattuck Hospital, Commonwealth of Massachusetts, Department of Public Health, Boston, Massachusetts.

in the same manner that the sheets are changed; or, alternatively, the orderly who is to move a litter patient may take a canvas stretcher with him and spread it over the litter before the patient is placed on it.

When this device was used in the X-Ray Department, the necessity for the orderly to make a judgment about the ability of a patient to stand or move by himself was eliminated by having every patient who needed a litter in order to get to the Department brought on a canvas stretcher. The decision to use the lift was then made in the Department.

A number of these canvas stretchers were available since they were easily made by the hospital sewing room. Soiling of stretchers due to accidents (as, for instance, those terminating barium enemas) was not a problem as they were easily laundered in the hospital.

It should be noted (Fig. 3) that, when the patient is lifted, there is considerable sagging in the canvas stretcher. This has three functions: (1) it prevents disoriented patients from rolling over the side; safety is further augmented, incidentally, by the position of the cradling device, which prevents the patient from sitting up; (2) when placed on an x-ray table, the excess material ensures that the rods fall over the sides and well outside the field to be roentgenographed; and (3) lateral roentgenograms can be obtained by placing the patient, suspended in the lift, against a wall-mounted film holder or against the table which has been rotated into the vertical position (Fig. 2). Excellent visualization of pleural fluid can be obtained in this way without effort by the patient.



Fig. 2. The device holding a patient for a lateral roentgenogram of the chest, using the table Bucky diaphragm.

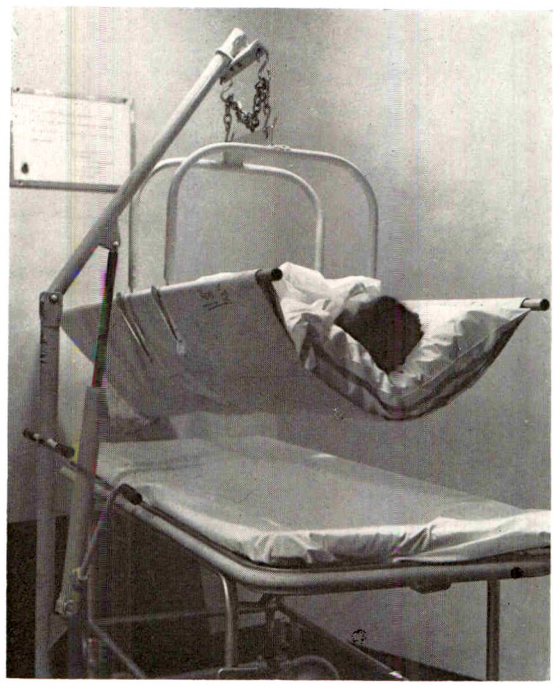


Fig. 3. Slack, built into the canvas stretcher, allows decubitus roentgenograms to be obtained without effort and gives the patient a sense of security.

Several other applications of this device have been worked out in our hospital. Bed patients can be weighed by inserting a spring scale between the boom and the center of the cradling device. Paraplegics, supported on a tighter stretcher, may be safely bathed in an ordinary bath tub.

Also, there appear to be obvious applications in other departments. The transfer of anesthetized patients from an operating table after a delicate operation is sometimes roughly performed. Similar handling

of patients delivered from the accident ward (with fractures, for example) does not help their treatment, yet up to now was unavoidable. This device can make patient handling in these circumstances safer for the patients and effortless for the personnel.

The device has been in service for over a year and, by performing the functions mentioned above, has gained considerable acceptance by patients, physicians, nurses and technicians.

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Lawrence Reynolds

1889-1961

EDITORIALS

Lawrence Reynolds and The American Roentgen Ray Society

With the death of Lawrence Reynolds, the American Roentgen Ray Society in particular and medical journalism in general have suffered a loss which will be felt for many years to come. Although Dr. Reynolds was a vigorous member and eminent President of this Society, as well as of several others, he will be best remembered for his immeasurable contribution as Editor of the American Journal of Roentgenology, Radium Therapy & Nuclear Medicine, the official organ of the American Roentgen Ray Society and the American Radium Society. Dr. Reynolds was first associated with the Journal as an Assistant Editor in 1928. In 1930 he became the editor and, until his death, he held that position continuously with the exception of the years 1947–1949 when he was President-Elect and President of the American Roentgen Ray Society. I doubt that anyone can really appreciate the amount of time and effort that Dr. Reynolds so selflessly gave to the Society in those thirty years, but the results are obvious to even the most casual reader of the Journal. Without exaggeration or fear of contradiction, one can truthfully say that the envious position which the Journal now occupies in the field of medical publications is, in a very large measure, due to the untiring, skillful and tactful editorial managing by Dr. Reynolds.

It can be stated that Dr. Reynolds was a "natural" for the position of Editor, for not only did he have the necessary intellectual interests and abilities but he also possessed limitless patience and great tact combined with a remarkable administrative capacity and a wonderfully warm personality.

Dr. Reynolds' avocations, too, were centered around literary activities and during his lifetime he assembled a valuable collection of rare and first edition medical books. A number of libraries throughout the country made use of Dr. Reynolds' wide knowledge and experience in activities of this sort and for years he served on the library governing boards of such institutions as Yale University, University of Michigan, Wayne County Medical Library Commission and the City of Detroit Library Commission.

The American Roentgen Ray Society knows full well that it can never adequately express its appreciation for Dr. Reynolds' years of distinguished and devoted service. Nevertheless, it does wish to record on this page in these few feeble words the position of great honor and affection he so rightly deserved and in which his memory will always be held.

John F. Roach, M.D.
Chairman of the Publication Committee

Resolutions of the Detroit Roentgen Ray and Radium Society

WHEREAS *the death of Doctor Lawrence Reynolds occurred on August 17, 1961 and*

WHEREAS *Doctor Reynolds was one of the earliest and most eminent members of this Society and*

WHEREAS *he brought renown to this Society by the excellence and multitude of his scientific productions and by his great ability as a teacher and as a practitioner of our profession and*

WHEREAS *his great energy and humanity and his concern for and excellent care of the afflicted served as an example for our membership and*

WHEREAS *he set a high standard for our practice and was at all times to us a teacher and friend, be it therefore*

RESOLVED *that his death be recorded in the minutes of this Society with a feeling of high regard for his memory and a deep sense of loss to all members of the Society, and be it further*

RESOLVED *that a copy of this memorial be submitted to the* AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY & NUCLEAR MEDICINE *and to* Radiology.

Lawrence Reynolds and Harper Hospital

WHEN Lawrence Reynolds was graduated from the Ozark, Alabama, high school in 1907, his teacher, Mary Newton, presented him with two volumes of Oliver Wendell Holmes' "The Autocrat of the Breakfast Table." Mary Newton's inscription read: "Lawrence: Acquire the genial humor, the ready wit, and the broad culture of the recondite old aristocrat."

That he succeeded in fulfilling Miss Newton's fondest hopes for him, all of his associates at Harper Hospital can affirm. It has been my privilege to serve as President of the Board of Trustees during the entire time of Dr. Reynolds' association with Harper Hospital and to observe his influence in our institution.

This young doctor, dedicated to a young specialty, came to us shortly after the conclusion of World War I. He lived and worked as an influential member of our "Family" from that time until his death. He was devoted to his patients, his profession, and to the welfare of this institution, and his devotion was enriched by "genial humor," "ready wit," and "broad culture."

These qualities gave him insight into problems frequently onerous to the practicing physician, problems like the practical ones of institutional organization which face a Board of Trustees. He knew, too, that the physician's ethics and ideals frequently impose conditions which perplex even the most informed laymen, like members of a Board of Trustees. He knew that each body needed interpretation to the other so that they could work together to fill their common purpose. And he was uniquely fitted, largely through practice of his old teacher's advice, to fill the function of interpreter. Dr. Reynolds, throughout his career at Harper Hospital, had an unusual comprehension of the legitimate interests of both. As Chief of our Department of Radiology, as well as in his later position as Chief of the Medical Staff, he worked ceaselessly for that ideal balance which inevitably results in institutional progress.

Illness was the only reason for his ever missing a meeting of the Board of Trustees during his tenure as Chief of the Medical Staff—and happily, there were very few such occasions. Ours was a long and pleasant association. He gave generously of his personal time and abilities to ensure that our mission could be effective in our community.

It was not only in his professional life that Dr. Reynolds was a man of "broad culture." His name could always be found in the list of sponsors of any worthwhile community endeavor. This was not a perfunctory listing, for where his name appeared, he was active, and his active participation served our hospital well. One always knew that Dr. Reynolds' interpretations of need, and recommended actions on behalf of the Medical Staff he represented, were based upon the ultimate welfare of the patient, and that he had carefully considered this in the light of his knowledge of our community, as well as in the light of the profession he served so well and faithfully. We are grateful that he was with us for most of his long and fruitful career, and we shall sorely miss him.

RICHARD H. WEBBER, *Chairman, Board of Trustees, Harper Hospital*

Lawrence Reynolds and Wayne State University



Doctor of Laws

June 11, 1956

LAWRENCE REYNOLDS,

a native of Alabama; a graduate of the University of Alabama in 1912, and of the Medical School of the Johns Hopkins University in 1916; he has carried on the private practice of roentgenology in Detroit since 1922, and for eleven years has been Professor of Radiology in the Wayne University Medical School. Since 1945 he has served as Chief of the Department of Radiology, and as Chief of Staff and Chairman of the Executive Committee of the Harper Hospital, Detroit.

Honored by his alma mater with the degree Doctor of Laws, and by radiological societies in Germany, Italy, and Colombia with honorary memberships, he has edited the *American Journal of Roentgenology*, *Radium Therapy*, and *Nuclear Medicine* since 1930.

Through the years he has brought together one of the world's great private collections of medical texts and treatises. Noted for his knowledge of library acquisitions, he is currently an Honorary Trustee of the Yale Medical Library Associates, a Member of the Committee of Management of the Clements Library of the University of Michigan, Chairman of the Medical Library Commission of the Wayne County Medical Society, a Member of the Grolier Club of New York City, and of the Harvey Cushing Society. As President of the Detroit Public Library Commission, he has brought to local problems the breadth of view and deep wisdom of his national experience.

Wayne University is proud to recognize the work of one of this country's greatest radiologists. His lifetime devotion to scholarly work as editor and bibliophile, his own research and his encouragement and training of young scientists, and his direction of the staff of a great hospital have helped to shape the whole course of modern radiological medicine.

IN THE passing of Lawrence Reynolds, the cause of scholarship and intellectual excellence lost a firm friend. His entire medical career was one in which the teacher, investigator, bibliophile and practitioner of the skills of radiology were artfully blended. His service to medical education was a long and varied one. When he returned from overseas service in World War I, he took a post as Instructor in Roentgenology at the Johns Hopkins University Medical School. This appointment so soon after graduation was indeed a rare thing in academic medicine in the period before 1930. The following year he went to Boston to Harvard and the Peter Bent Brigham. He remained in Boston as roentgenologist at the Brigham and Instructor in the Harvard Medical School.

In 1922 Dr. Reynolds came to Detroit and entered the private practice of roentgenology. However, this activity gave him only partial satisfaction. The world of books and the world of learning which had captured his attention as a youngster would not be denied. Along with his busy professional life, he began to collect those volumes which are now the care of the Reyn-

olds Library in the University of Alabama. His knowledge of medical history grew with the library. His fine discrimination and his desire to achieve perfection made it possible for him to assemble a collection which contains the finest copies extant of many of its items.

In 1945 Dr. Reynolds was appointed Professor of Radiology and Chairman of the Department of Radiology in Wayne State University. He served the University well for seven years. In this time he brought to life a department which had suffered through the agony of World War II as well as chronic budgetary inanition. When this had been done, he urged the prompt appointment of his successor and resigned as Chairman of the Department. He continued to serve the University as Clinical Professor of Radiology until his seventieth year when he became Professor Emeritus. He brought great distinction to the College of Medicine and faithfully attended to his duties as teacher, especially in the areas of graduate instruction and resident education.

In recognition of his great attainments in the world of books, his service to the Public Library of Detroit, the Yale Medical Library, Clements Library of the University of Michigan and to Wayne State University, Dr. Lawrence Reynolds was granted the degree of Doctor of Laws in 1956. This was but one of many honors which came to him the last fifteen years of his life. He deserved them all. His colleagues will long remember him with respect and affection.

GORDON H. SCOTT, *Vice President for Medical College Development and Dean, College of Medicine, Wayne State University*

Lawrence Reynolds as a Teacher

"I WILL share my precepts, oral lessons, and any knowledge with my sons, with those of my master, and with pupils bound by a promise and an oath in accordance with medical law." A covenant injected into the medical conscience of all of us by Hippocrates, unrequited in the activities of many, but accepted each day by Lawrence Reynolds, M.D. As a proponent of the swift accurate interpretation of the roentgen shadow, he certainly taught all by example.

And yet, teaching was more to him than this.

At some time during his long career he became imbued with the importance of diffusing medical learning. Perhaps this developed as he read to his blind physician father in rural Alabama. A frequent text was Sir William Osler's "Principles and Practice of Medicine." The latter's views on teaching were strikingly similar to his own. "Replace the Chinese with the Greek spirit, enable him (the student) to seek knowledge for itself . . . the pupil and the teacher working together on the same lines, only one a little ahead of the other." Dr. Reynolds approached education as though he felt that teaching was the perpetual Messiah of medicine; the constant connection between the established and the aspiring, the bond between accepted fact and better ideas. He cultivated the ability to instill an intellectual respect within the student without pre-empting questions or rebuttal. He knew how to sustain the interest of his residents, plant the seeds of original investigation, or at times to spoon feed when this was the most expedient kind of informative nutrition. His greatest talent was his ability to prevent his mere presence or renown to persuade or unduly influence his residents or students. He chose to counsel, but not to overawe.

Training in radiology began at Harper Hospital in 1920. Somewhat later a formal residency program was inaugurated. For many years punctually at 7:30 A.M., residents and, subsequently, students from the Wayne State College of Medicine clustered about Dr. Reynolds in the reading room. These sessions usually lasted for two or three hours. He disdained the formal lecture, preferring the spontaneity of the day's cases for his teaching purposes. Protocol was limited to the painless introduction of the neophyte into the discussion with "Would you continue to employ this man with a chest that looks like this?" He was the faculty and all of radiology was his curriculum. His film descriptions were always punctuated with shrewd clinical insights or embellished by the recall of a conversation with Drs. Harvey Cushing, Henry Christian or some other titan. The mornings were further enriched by his lore of the history of radiology and colorful sketches of its pioneers. Retelling one of Sir William Osler's stories about himself, he pointed out the importance of a circumspect differential diagnosis. Shortly after Dr. Osler came to Baltimore he was asked to see an elderly and important gentleman. Examination

revealed a large pelvic tumor, and a diagnosis of inoperable sarcoma of the pelvis was promptly made. As gently as possible Dr. Osler explained the condition to the patient's wife and advised that a surgeon see the case. The same day the surgeon came and removed the tumor with a catheter. Similar pointed, often humorous stories usually adjourned our meetings.

He schooled his residents in good radiologic manners and practicality. His maxims were simple. Courtesy should be the trademark of the radiology department. Service is the prime consideration extended to the attending physician. Examinations should be conducted quickly with initial accuracy. We were always cautioned to examine and talk to the patient so as to be able to extract the most from the roentgenograms. He once said that a radiologic report should read like the Egyptian Rosetta Stone: meaningful to all who might have occasion to peruse it.

As a Charter Diplomate of the American Board of Radiology he was well acquainted with the scope and aims of its certifying examinations. He had a recurring penchant for keynoting the diagnostic entities and procedures likely to be emphasized from time to time. Grooming such as this helped to lessen the incubus of intensive study and provided the tangible tools for shaping a profitable plan of preparation.

A certain filial charm fitted him well for his role as Professor of Radiology at The Wayne State University College of Medicine. The young men, many of whom affiliated with the program largely because of Dr. Reynolds, rightfully came to expect his facile solutions to their most perplexing medical and personal problems. He was adviser, confidant and intercessor to many. In those interns, students and residents merely passing through the x-ray department, he tried to create an appreciation for the proper place of radiology in the spectrum of medical specialties and for the role of the radiologist in the care of the patient.

The literature abounds with his medical papers and editorials, and these, too, serve to convey knowledge. They cannot supplant the daily *vis-à-vis* contact we had with this superb radiologist. He was available. He was approachable. His time was not of the essence. He never spoke from a professorial whirlwind. He passed the baton of knowledge with the grace of an Olympian.

In journeyman fashion our local newspapers concluded, "Doctor Reynolds leaves no immediate survivors." More correctly, he left none who survives him only immediately. Some of us are his disciples; some his ambassadors, a very few may become his peers. We all have a legacy in his encouragement to try to learn something from everyone. Through his teachings we link him with tomorrow. In the words of Henry Adams, "A teacher affects eternity; he can never tell where his influence stops."

JAMES J. SNIDER, M.D., *Former Medical Student, Wayne College of Medicine and Assistant Radiologist, Harper Hospital*

The Lawrence Reynolds Library*

On Sunday afternoon, February the Second 1958, The Lawrence Reynolds Library was dedicated by impressive ceremonies at the University of Alabama Medical Center in Birmingham. This Library, which contains one of the world's finest and most valuable private medical collections, was donated to his Alma Mater and his native state by Dr. Lawrence Reynolds, Editor of this Journal, who spent a lifetime acquiring it.

This rare collection is housed in a special wing which the University has built as an extension to its new Medical Center Library. It consists of nearly 6,000 individual pieces of original manuscripts, autographed letters and old medical books, some of them dating back to the fifteenth and sixteenth centuries, representing samples of highest achievement in Renaissance printing.

The section of original manuscripts includes, among others, the fourteenth century manuscripts of Arnoldus de Villa Nova entitled *Regimen Sanitatis ad regem Aragonum* and John of Toledo's *Dietarium*; the original manuscript of the article on *The Stereoscope and Stereograph*, contributed to the *Atlantic Monthly* in June, 1859 by Oliver Wendell Holmes; and, of the more recent ones, the address on *The Discovery of Radium* by Mme Marie Curie (Sklodowska) delivered on May 14, 1921 at Vassar College, Poughkeepsie, New York, with an autographed photograph.

The letter section contains all the correspondence of Louis Pasteur with the Mayor of the village on silk worm disease, consisting of 20 holographic letters of Pasteur (1866–1889), 8 letters in the hand of Mme Pasteur, and 2 unpublished photographs; the letter of Louis Pasteur to Monsieur Marchand, dated August 12, 1881, on rabies; and other items from the pen of this giant of science who revolutionized both industry and medicine by applying laboratory knowledge to fight disease. There are also signed letters with typed transcripts by Sir William Osler to his "good friend Ned Milburn" (1865–1919), and two original letters from Wilhelm Conrad Röntgen and Frau Wilhelm Conrad Röntgen to Louis Grauel; and others.

Of the large section of medical books of the sixteenth and seventeenth centuries, three groups deserve special mention. It is now generally agreed that the foundations of modern medicine were laid down in this period by three epoch-making contributions. In 1543 the first complete text book on human anatomy was published by Andreas Vesalius entitled *De humani corporis fabrica librorum epitome*, Johannes Oporinus, Basel. This book, as well as Vesalius' other contributions, was illustrated with magnificent drawings by van Calcar, a pupil of Titian. The Library contains not only Vesalius' textbook in its first edition but also other works of the truly great anatomist, several later editions of his works and a group of books on the works of his

* Reprinted from: Am. J. Roentgenol., Rad. Therapy & Nuclear Med., April, 1958, 79, 726–727.

teacher, Sylvius, who from a friend turned into a bitter foe, of Fallopius and Eustachius, his successors, and of other famed anatomists of the period, most of whom became "Vesalius converts." This study of the "fabric" of the human body based on pure research was soon followed by an interest based on similar ground in the functions of the human body. Among those who pursued such a course was Andreas Caesalpinus, who, in his *Peripateticarum Questionum Libri Quinque* published in Venice in 1571, began speaking of the "circulation" of the blood. His bold theory, however, was not supported by experimental proof and thus he had no influence on his contemporaries. Later in 1628, at the book fair in Frankfurt, a slender, poorly printed volume was displayed by William Harvey on the *Exercitatio anatomica de motu cordis et sanguinis animalibus*, presenting for the first time experimental proof that the heart acts as a pump causing circulation of the blood throughout the body. The books of Caesalpinus and Harvey and 12 other texts and facsimiles of the book of Harvey published in different countries form the nucleus of the second group of works, containing the contributions of Fabricius Hieronymus of Aquapendente, Harvey's teacher, on *De venarum ostiolis;* of Francis Bacon, one of Harvey's most notable patients, on *Instauratio magna* (*Novum organum*); Harvey's second great work *Exercitationes de Generatione Animalium* (1651) on embryology and many similarly rare items. The third group of collections of this period is highlighted by works of Ambroise Paré, the greatest surgeon of the sixteenth century. Paré based his practical surgery on the new concepts expounded in Vesalius' *De Fabrica* and, after being able to conquer the prejudices of the time, introduced sound methods for the treatment of a rather significant number of lesions. His influence on contemporaries and successors for the next two centuries is amply reflected by the many contributions comprising this group.

In 1600, William Gilbert published his epochal work *De magnete, magneticisque corporibus et de magno magnete tellur; physiologia noua, plurimis argumentis experimentis demonstrata*, establishing the basis for the formidable sciences of magnetism and electricity, which were to develop. The early progress was rather slow until the middle of the eighteenth century when Benjamin Franklin in his extensive *Experiments and Observations on Electricity Made at Philadelphia* defined "positive" and "negative" electricity and considered, among many other things, the possibility of curing palsy by electric shock. In 1786 Luigi Galvani discovered "animal electricity." This was followed in rapid succession by Alessandro Volta's construction of the first electric pile, as communicated in a letter to the Rt. Hon. Sir Joseph Banks (1800); by Hans Christian Oersted's *Experimenta circa effectum conflictus electrici in acum magneticum* (1820), establishing a link between electricity and magnetism; by André Marie Ampère's *Mémoire présenté à l'Académie Royale des Sciences sur l'action mutuelle entre deux courants électriques* (1820), describing the mutual effect of two electric currents; and by G. S.

Ohm's work in 1827, formulating the relationship between voltage, amperage and resistance. Then in 1837, Faraday and Henry discovered electromagnetic induction. These important works and many others in the chain of development of the two sciences form an eminent part of the Library and constitute a monumental introduction to the vast collection of more recent contributions in the field of radiology.

Among the more recent contributions are also many rare works from other branches of medicine, as exemplified by some 40 writings from the pen of Sir William Osler, the great physician of modern times; an almost complete set of Harveian Orations, beginning in 1865; an extensive compilation of Nobel Prize Papers; and others.

These are but brief heuristic glimpses into a magnificent Library. It is written on the dedication plaque that graces its entry: "Each time one of you reaps from the great minds of the past the desire for finer achievement in your profession and nobler development of your own character, The Reynolds Library will have been rededicated." In the ancient words of Terentianus Maurus spoken in 1286, *Pro captu lectoris habent sua fata libelli.*

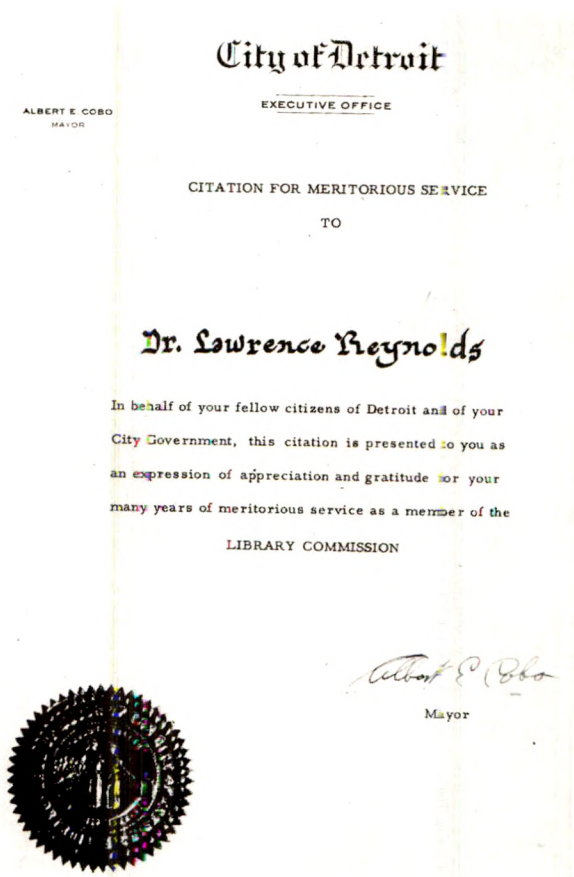
TRAIAN LEUCUTIA

Lawrence Reynolds and the Detroit Public Library

IN DECEMBER of 1960, Dr. Lawrence Reynolds, for the third time, completed a term as President of the Detroit Library Commission. It is indicative of his thinking that the final paragraph of his last presidential report included this quotation:

"*What may be emerging as a mark of our own generation is a widespread renewal of concern for the quality and intellectual aims of education.*"

This statement, quoted from Jerome S. Bruner, appealed to Dr. Reynolds because for the seventeen years during which he served as a member of the Detroit Library Commission he consistently supported every effort to make this Library one which was distinguished for excellence in its book collections and in its service.



City of Detroit

EXECUTIVE OFFICE

ALBERT E. COBO
MAYOR

CITATION FOR MERITORIOUS SERVICE

TO

Dr. Lawrence Reynolds

In behalf of your fellow citizens of Detroit and of your City Government, this citation is presented to you as an expression of appreciation and gratitude for your many years of meritorious service as a member of the

LIBRARY COMMISSION

Albert E. Cobo

Mayor

Dr. Reynolds was first appointed to the Detroit Library Commission in 1944, to fill an unexpired term, and was reappointed to six-year terms in 1949 and 1955. Thus he was just completing seventeen years of continuous service, more than any other current Library Commissioner, when his death occurred. The years spanned by his service were unusually important ones for the Library: the departmentalization of the Main Library was completed with the establishment of five new departments; ten new branch libraries were erected; a $500,000 service building was built to house the Library's extensive building maintenance shops and its large book bindery; and finally, after years of striving to have the beautiful Main Library enlarged, construction of a ten-million-dollar addition was started. It is regrettable that he didn't live to see the building occupied, which it is anticipated will be about a year from now.

Though he recognized the need for adequate buildings for the Library, his

interests were largely centered on books and their use. He revered fine books, and frequently visited the Rare Book Room; he respected the printed page of any book whose author had integrity and competence, and he had an active interest in trying to make library service available to adults and children, to scholars and beginners, to specialists and to those whose reading is broad in scope. It is interesting to note that while he was busily studying the library's books on small country libraries, with a view to helping his home town, Ozark, Alabama, develop a sound beginning for a community public library, he was also involved in providing a firmer base of support for the medical library in Detroit. The culmination of the latter is best covered by quoting from his 1949 report as President of the Detroit Library Commission:

"*The support, administration, and function of the Medical Science Library having become more and more confused through the years, it was finally decided by the Detroit Library Commission that the best interest of the people of the City of Detroit would be realized by putting its 51,000 volumes under the management of the Medical School of Wayne University. . . . By the accomplishment of this transfer, the sole responsibility for the care and maintenance of this Medical Science Library rests with the Medical School of Wayne University.*"

The instrument of transfer, however, at Dr. Reynolds' insistence, contained assurance that the Medical profession of the Detroit area should always have free and ready access to the Medical Science Library.

Quite apart from whatever his accomplishments were in his chosen profession, he was a person who quietly and unselfishly assumed more than his full share of obligations to society in general.

In manner, Dr. Reynolds has been described as courtly. An innate graciousness, a sensitive consideration for the feelings of others, and a pleasant, quiet dignity characterized him at all times. These fine qualities were as evident to the building guards and the elevator operator as they were to the administrators and the Commissioners of the Library.

Within days after his death, a very beautiful tribute from a non-medical professional acquaintance in New York was received. Two paragraphs of that letter are quoted here, as they pay tribute to him as an outstanding person who distinguished himself in service given beyond his own profession.

"*He was a man of culture, intelligence, energy and breadth of vision, and therefore highly qualified as a member of the Library Commission.*

"*This physician typified to me what a fully developed human being should be, and it is comforting to realize that the human race from time to time can produce such an outstanding scholar and citizen.*"

RALPH A. ULVELING, *Director, Detroit Public Library*

The Heritage of Lawrence Reynolds

A MAN'S heritage may in part determine his course through life. Many, imbued with the finest of inheritance, fail to appreciate its value, to utilize it, enhance it and to pass it on with enrichment to those who follow. Few men have succeeded so admirably in nurturing and embellishing an already rich heritage as did Dr. Lawrence Reynolds.

Born in lower Dale County, Alabama, Dr. Reynolds was reared among gracious, hospitable people in the post reconstruction period of our nation's history. That this portion of his heritage may have been changed is related in an anecdote known to his family and pertains to the emigration from the State following the Civil War. Two such movements occurred,[1] the first culminating in 1869 and the second in 1873–1874 with most of the emigrants going to Texas, while others went to Brazil, Mexico, the North, Tennessee and Georgia. It was estimated at that time that the State lost more of its population by this emigration than by the effects of the war itself. Dr. Reynolds' grandfather, it is said, may have been prompted to participate in this emigration but was induced to stay in his beloved Alabama to care for the local populace.



The Reynolds family[2] is descendant from English and Welsh immigrants to this country in the early seventeenth century who settled on the Rapidan River, Isle of Wight County, Virginia in about the year 1637. An ancestor, George Reynolds, was born in 1555 in County Kent, England and gave issue to some children who settled in Virginia while others came to the New England states. Two well known descendants of George Reynolds were Samuel Langhorne Clemens, known to all the world as Mark Twain, and Nancy Witcher Langhorne who later became Lady Astor. Dr. Reynolds shared his family heritage with these distant cousins along with many distinguished military officers and other persons of eminence.

The Reynolds coat of arms, the proud possession of a great family, had its beginnings in the days of antiquity. The family's ancestry is traced to Norman origins claiming descent from Reynolds, son of Greyferth—The

[1] Civil War and Reconstruction in Alabama. Walter L. Fleming, Columbia University Press, New York, 1949.

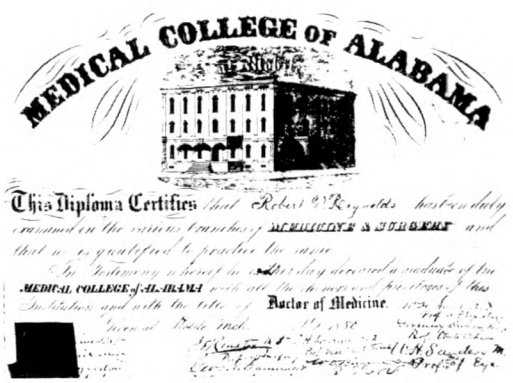
[2] Reynolds Family—1530–1959. The Goetz Company, Washington, D. C., 1959.

Dane—King of Northumberland. Greyferth and his two sons were driven from England about 944 A.D. and took shelter in Normandy. Fitzreynolds (meaning son of), one of the sons of Reynolds, returned to England with William the Conqueror.[2]

Dr. John Adams Reynolds, Lawrence's paternal grandfather, was born in 1819 in North Carolina and moved to Alabama at the age of seventeen, later practicing medicine there for a period of forty-seven years. His medical diploma from a school in Cincinnati is dated February 23, 1845. He died in 1891, two years after Lawrence's birth and, therefore, the grandfather's heritage of medicine was handed down through his son, Dr. Robert Davis Reynolds, born in Alabama in 1845, who had his preliminary medical education in Mobile in 1872, just seven years after the close of the Civil War.

"Dr. Bob" served as a First Sergeant, Company F, 6th Alabama Cavalry, having enlisted in April, 1863 at the age of sixteen in T. A. Abercrombie's Division. After his return from the war, Dr. Bob went to the medical school in Mobile and in 1872–1873 practiced with his father at Skipperville in Dale County until the fall of 1880 when he returned to the Mobile Medical School and graduated with the degree of M.D. He then practiced in Skipperville for nineteen years, subsequently moving to Ozark, Alabama. Dr. Robert Davis Reynolds was blind throughout a large part of his professional life. Thus

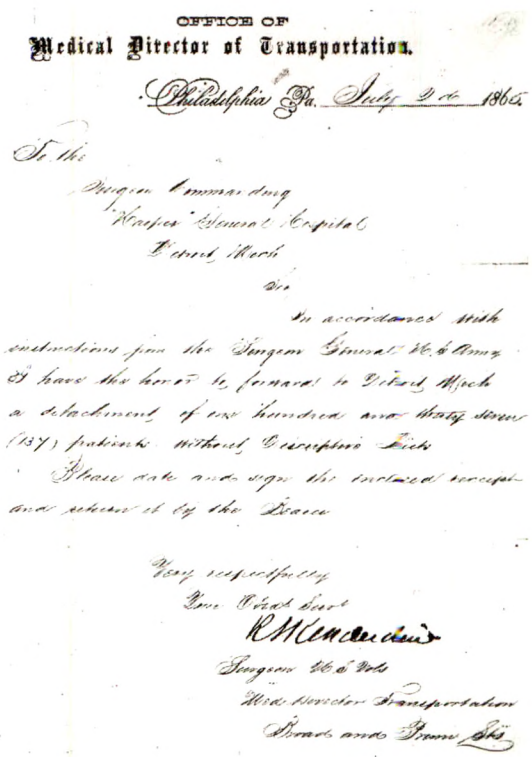

To the Friends and Patrons of Science
AND OF
MEDICAL REFORM,
The Botanico Medical College of Ohio send
GREETING.


MEDICAL COLLEGE OF ALABAMA
This Diploma Certifies
Doctor of Medicine

young Larry became his father's eyes as he went about his rounds. Exposure to the practice of medicine in this somber and impressive way reminds us of Sir William Osler's "The Student Life," in which he states "Amid an extreme heritage of sorrow and suffering our work is laid." Undoubtedly this is the medical heritage which induced Lawrence to become a physician, one who never lost the warmth that is so necessary in the proper care of the sick. Lawrence Reynolds went to the Johns Hopkins Medical School in 1912, subsequently entered World War I, returned to Johns Hopkins, and later became associated with Peter Bent Brigham Hospital and Harvard University in Boston. In 1922 he came to Harper Hospital in Detroit.

Harper Hospital had its birth during the War between the States and it was through Dr. Reynolds' interest in this conflict that a copy of an original order from the Surgeon-General of the United States Army, dated July 26, 1865, to convey a detachment of 137 soldier-patients to the "Harper" U.S.A. General Hospital was procured and presented to the historical collection of the Harper Library.

Originally Harper Hospital was a series of eleven frame buildings facing Woodward Avenue. At the end of the war, a local Board of Trustees assumed control of the hospital with the provision that Civil War soldiers would continue to be cared for.



OFFICE OF
Medical Director of Transportation.

Philadelphia Pa. July 26 1865

To the
Surgeon Commanding
Harper General Hospital
Detroit Mich

Sir

In accordance with instructions from the Surgeon General U.S. Army I have the honor to forward to Detroit Mich a detachment of one hundred and thirty seven (137) patients without Descriptive Lists

Please date and sign the inclosed receipt and return it by the Bearer

Very respectfully
Your Obed Svt
R. Mc Sherrell
Surgeon U.S.A.
Med Director Transportation
Board and Room 1865

Later, in 1863, Harper Hospital became the site of the Detroit Medical College, the first medical school in the City, utilizing two of the eleven buildings. In January, 1884 the Children's Free Hospital Association was formed and Harper Hospital served as the first children's hospital until December, 1886 when the facilities at Harper were outgrown and a new location was obtained on West Fort Street. An early lying-in facility, later resulting in the formation of Woman's Hospital, was also initiated at Harper Hospital. Still other institutions, such as St. Luke's Hospital and Church Home in 1867, had their beginning at Harper Hospital.

Thus Dr. Reynolds became associated with a hospital which later was to achieve eminence among American hospitals but had its roots in the Civil War. The writer was privileged to be along with Dr. Reynolds, a charter member of the Harper Hospital Civil War Study Club, organized on February 12, 1958.

Dr. Reynolds' ability to enrich his heritage is further manifested by his affectionate relationship with the scholarly Dr. Hickey, whom he first met in the European Theater of World War I and who was the Founder and First Editor of this JOURNAL which Dr. Reynolds then subsequently edited for a period of over three decades.

From this great inheritance of family, the South, the medical institutions

with which he was early connected, and his associates, Dr. Reynolds brought to his professional life charm, warmth and enthusiasm which have been an inspiration to many. Sir William Osler has said, "No bubble is so iridescent or floats longer than that blown by the successful teacher." Dr. Reynolds has blown many such bubbles in his illustrious career. To those of us privileged to have been associated with him the words from Psalms 16, Verse 6 are particularly pertinent, "The lines are fallen unto me in pleasant places; yea, I have a goodly heritage."

KENNETH L. KRABBENHOFT

Lawrence Reynolds—An Homage

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE in its October, 1961 issue regretfully announced the death of its distinguished Editor, Dr. Lawrence Reynolds, which occurred on the evening of August 17, 1961 in Detroit, Michigan. The end came suddenly, with quiet grace and dignity, as he would have wished it to be—befitting his gentle nature and noble character.

Lawrence Reynolds was born February 11, 1889 in Skipperville, a charming community near Ozark, Alabama. He was the eighth of nine children of Dr. Robert Davis Reynolds, Sr., a practicing physician of that community, and of Mary Frances Card. Two of his brothers, John Leonard Reynolds and Robert Davis Reynolds, Jr., as well as his grandfather, John Adams Reynolds, were also physicians. This excellent family background afforded him a wisely directed early education which undoubtedly carried the seeds of a brilliant medical future. After graduation from the Ozark High School in 1907, he attended the University of Alabama and in 1912 received the degree of Bachelor of Arts.

During these formative years of Lawrence Reynolds, the elder Reynolds gradually lost his eyesight and from the age of twelve the inseparable son became the "eyes" of his beloved parent, driving his horse and buggy on house calls, writing out his prescriptions and acting generally as his most trusted adviser. The cultured father was a great admirer of classical literature and was keenly interested in Sir William Osler and other contemporary medical giants, so young Lawrence did the thing that would give his father the most pleasure—he read to him night after night the texts that he was so fond of hearing. This beautiful expression of filial attachment imperceptibly ripened into an inquisitive appreciation and love of his progenitors' noble profession and the fall of 1912 found Lawrence Reynolds at the Johns Hopkins Medical School, eager to absorb knowledge from such famous men as William H. Welch, William S. Halsted, Joseph C. Bloodgood, Hugh Hampton Young, Howard A. Kelly and others.

In June, 1916, upon receiving his M.D. degree, he timidly approached Dr. Frederick H. Baetjer, Professor of Radiology of that renowned institution, and within a short time became his first resident, thereby starting on an unexplored trail which was to blaze for him so brightly later.

In May, 1917, restless, now radiologically indoctrinated, young Lawrence was ready to move again, this time overseas with the American Ambulance Service, to care for the suffering soldiers in the European Theater of War. In view of the fact that the Department of Radiology was under the administration of the Department of Surgery, it was necessary for him to obtain "clearance" from the Chief, Doctor Halsted. This was granted rather reluctantly, with the provision that within six months he would return to his old post.

In the meantime, World War I had reached the climax in its fury. Captain Lawrence Reynolds remained with the A. E. F. for two years. During this period it was his good fortune to be the recipient at the American Ambulance Hospital No. 1, later called the American Military Hospital No. 1, of the first Coolidge tube overseas which later was to revolutionize therapeutic radiology. This tube was presented for inspection by him to General Pershing on his visit to the hospital.

Another of his good fortunes, and undeniably the most fateful event in his life, was to meet, while in the European Theater of War, among the many Allied radiologic celebrities, our own Major Preston M. Hickey, who went to France with the American Expeditionary Forces early in 1917 as roentgenologist with the Harper Hospital Unit—one of the first to be sent overseas. Major Hickey was early detached from that duty and assigned to the larger duty of Consultant in Roentgenology, visiting the base areas throughout France as an adviser to those charged with administration of the x-ray work in the entire A. E. F. In this capacity, Major Hickey often visited the American Military Hospital No. 1 and always found Captain Reynolds hard at work, performing his exacting duties with faithful thoroughness, yet with a genial manner and complete equanimity. These comradely meetings under difficult circumstances later led to an enduring friendship and an extremely valuable collaboration between the distinguished Founder and the tridecennial Editor of this JOURNAL.

In May, 1919, Lawrence Reynolds returned to the Johns Hopkins Medical School, as promised, although at a later date than anticipated. He was made Instructor in Radiology with an assurance of rapid advancement on the ladder of academic promotions. As early as October, 1919, however, his quest for knowledge drove him to still newer grounds. Like the Medieval European student, who magnetized by the professors of a given institution, roved from one University to another, Dr. Reynolds was now found at the Peter Bent Brigham Hospital in Boston, where the celebrated Henry Christian and Harvey Cushing were the main attractions. From October, 1919 to May, 1922 he was Roentgenologist at that Institution and from July, 1920 to May, 1922 he was teaching as Instructor in Roentgenology at the Harvard Medical School. Yet, during these very important and fruitful years of his life, he could not forget Major Hickey, his great friend of the American Expeditionary Forces, and Preston M. Hickey could not forget the brilliant young radiologist whom he met overseas.

When, in 1922 Doctor Hickey was appointed Professor of Radiology at the University of Michigan in Ann Arbor, and abandoned the private practice of radiology, he used all his influence to persuade this brilliant young radiologist to join the organization that he founded in Detroit in 1900. It was an auspiciously fortunate day for this organization, which already had the benefit of the administrative genius of Dr. William A. Evans, that Dr.

Reynolds accepted the offer and in May, 1922 became the third member of the partnership, with the name of Drs. Hickey, Evans and Reynolds.

From 1922 until his death Dr. Reynolds practiced and was a most ardent disciple of private radiology, advantageously supported and enhanced by scientific investigations and academic teaching. His innate qualities of friendliness, graciousness, and sympathetic concern for the welfare of his patients were transcended only by his gentleness, charitableness and unbounded generosity.

After the retirement of Dr. Hickey from the partnership, the organization was known under the name of Drs. Evans and Reynolds, and, since the death of Dr. Evans in 1940, it has carried the name of Dr. Lawrence Reynolds and Associates.

Dr. Reynolds was appointed to the staff of Harper Hospital in 1922 and successively became Chief, Department of Radiology, Harper Hospital (1940); Professor of Radiology, Wayne University, College of Medicine (1945–1952); Clinical Professor of Radiology, Wayne State University, College of Medicine (1953–1959); Emeritus Professor of Radiology, Wayne State University, College of Medicine (1960–1961); and Visiting Professor of Radiology, University of Alabama Medical College (1960–1961). In addition, for many years he had been a Consultant in Radiology on the staffs of several other hospitals in Detroit.

In 1945 and from 1948 to 1959 he was Chief of The Medical Staff, Harper Hospital and Chairman, Executive Committee, Harper Hospital.

Dr. Reynolds was a member or fellow of numerous medical societies. He was Past President of the Detroit Roentgen Ray and Radium Society, Detroit Medical Club, Detroit Academy of Medicine, American Roentgen Ray Society and American College of Radiology.

Dr. Reynolds had received the honorary degrees of Doctor of Laws from the University of Alabama (1949) and the Wayne State University (1956); and the Honorary Citation of the Michigan State Medical Society (1959). He was an Honorary Member of the Radiologic Societies of Germany, Italy and Colombia. He was a Pancoast Lecturer (1941), Caldwell Lecturer (1944), Gold Medalist of the Radiological Society of North America (1956) and Gold Medalist of the American College of Radiology (1960).

The great American heritage and the uniquely cultural background of Dr. Reynolds laid the foundation, unconscious to himself in his consecration to ideals, for an inspired bibliophile, authoritative librarian and eminent scholar.

His bibliophilistic inclinations were already manifested during his assignment to the European Theater of War, when in his spare moments—as few as they were—he would prowl in sheltered book-shops along the Seine or visit fascinating galleries in more secure abodes to find some "antique books" of medical interest. These heuristic pursuits, which were assiduously followed throughout his lifetime resulted in one of the world's finest private collections

of medical texts, old original manuscripts and rare holographs. It was undoubtedly the greatest moment of his life when on February 2, 1958, in Birmingham, Alabama, at the dedication of The Lawrence Reynolds Library, which appropriately was named in his honor, he could say: "A diploma from the University of Alabama graced my wall for many years and everytime I looked at it, I felt greatly indebted; so I am returning it to you with this handful of books." This "handful of books" was a half-million dollar collection of early editions of works of some of the greatest medical and scientific pioneers of the fifteenth through the nineteenth centuries. At these impressive dedicatory ceremonies, Mr. Hill Ferguson, Chairman of the Board of Trustees, University of Alabama, presented Dr. Reynolds with a bookplate bearing the family coat of arms, which is to appear on all the books of this library.

Dr. Reynolds' inborn reverence for books made him particularly qualified to serve on library commissions with authoritative knowledge. He was an enthusiastic member, trustee or adviser of several of the famous medical libraries in various parts of the country and he was extremely proud of the fact that he was the "Library Commissioner with the longest tenure of service to the City of Detroit." On January 22, 1957, he was awarded by the late Mayor Albert E. Cobo the Citation for Meritorious Service.

In his devotion to scholarly work as writer, reviewer and editor, Dr. Reynolds exerted unbelievable steadfastness, always inspired by advancing progress through unceasing search for truth. He contributed to the medical literature numerous articles on important original investigations, countless reviews with unusually keen analytic appraisal and for over three decades he was the illustrious Editor and leading spirit of the AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE. In 1956, on the occasion of the Fiftieth Anniversary of this JOURNAL he, with characteristic self-effacement, admirably described why it had become one of the leading radiologic periodicals of the world. "The founder and first Editor of the Journal, Doctor Hickey," wrote Dr. Reynolds, "blazed the trail of a high standard of scientific endeavor from which the Journal has not deviated. The Societies, the Editorial Staff, the Publisher, Mr. Charles C Thomas, and the Printer, the Banta Publishing Company, have combined their efforts in producing a scientific Journal of distinctive quality. The American Roentgen Ray Society and the American Radium Society can take justifiable pride in the splendid position which their official Journal occupies today."

Dr. Reynolds, possessed by an extremely friendly nature, approached his task graciously and accomplished it with ingenuity, vision and charm. As a famous bibliophile, authoritative librarian, eminent scholar, and foremost of all as a great radiologist, he always remained an inspiringly genial man His amazing achievements—to quote from the honorary L.L.D. citation of Wayne State University—"have helped to shape the whole course of modern radiological medicine."

TRAIAN LEUCUTIA

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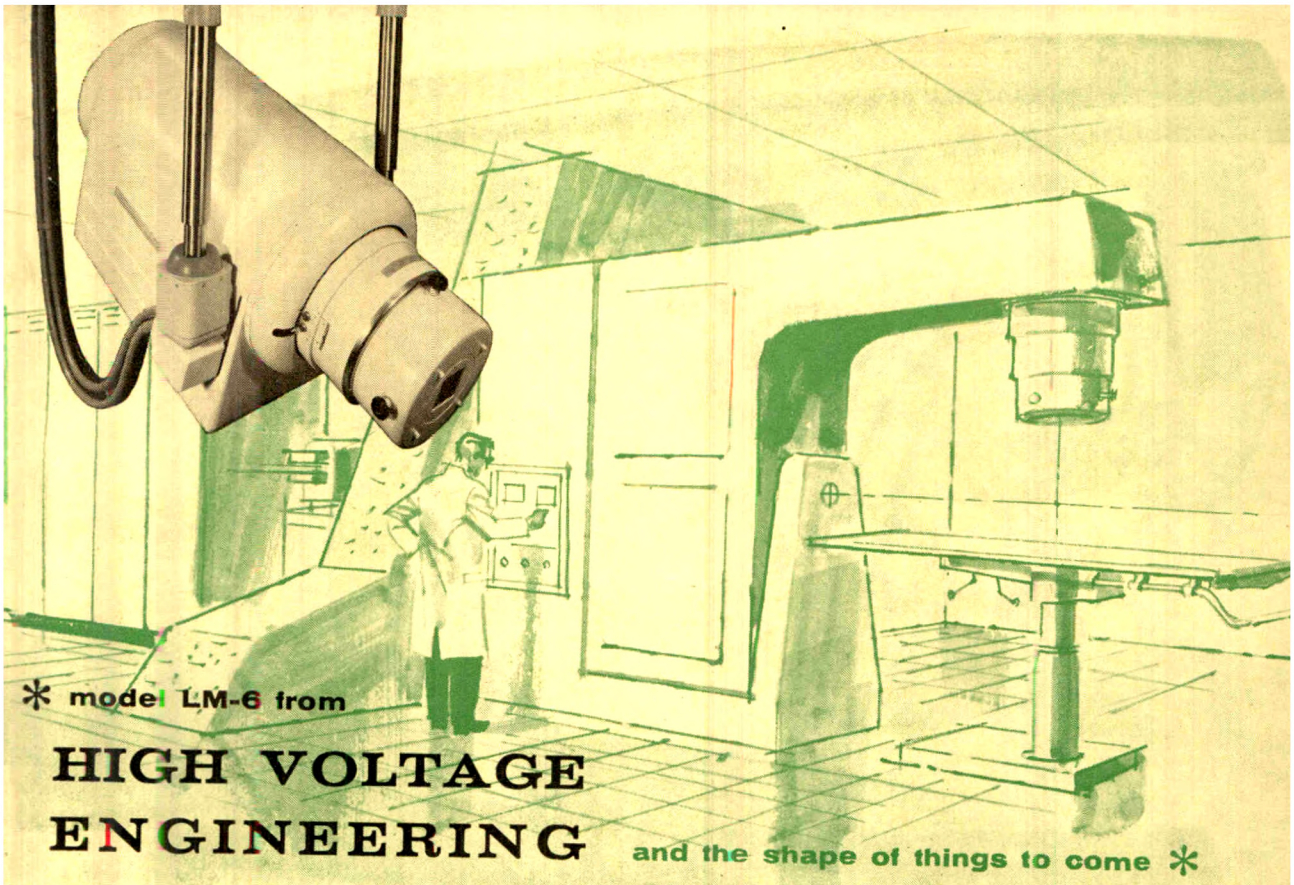
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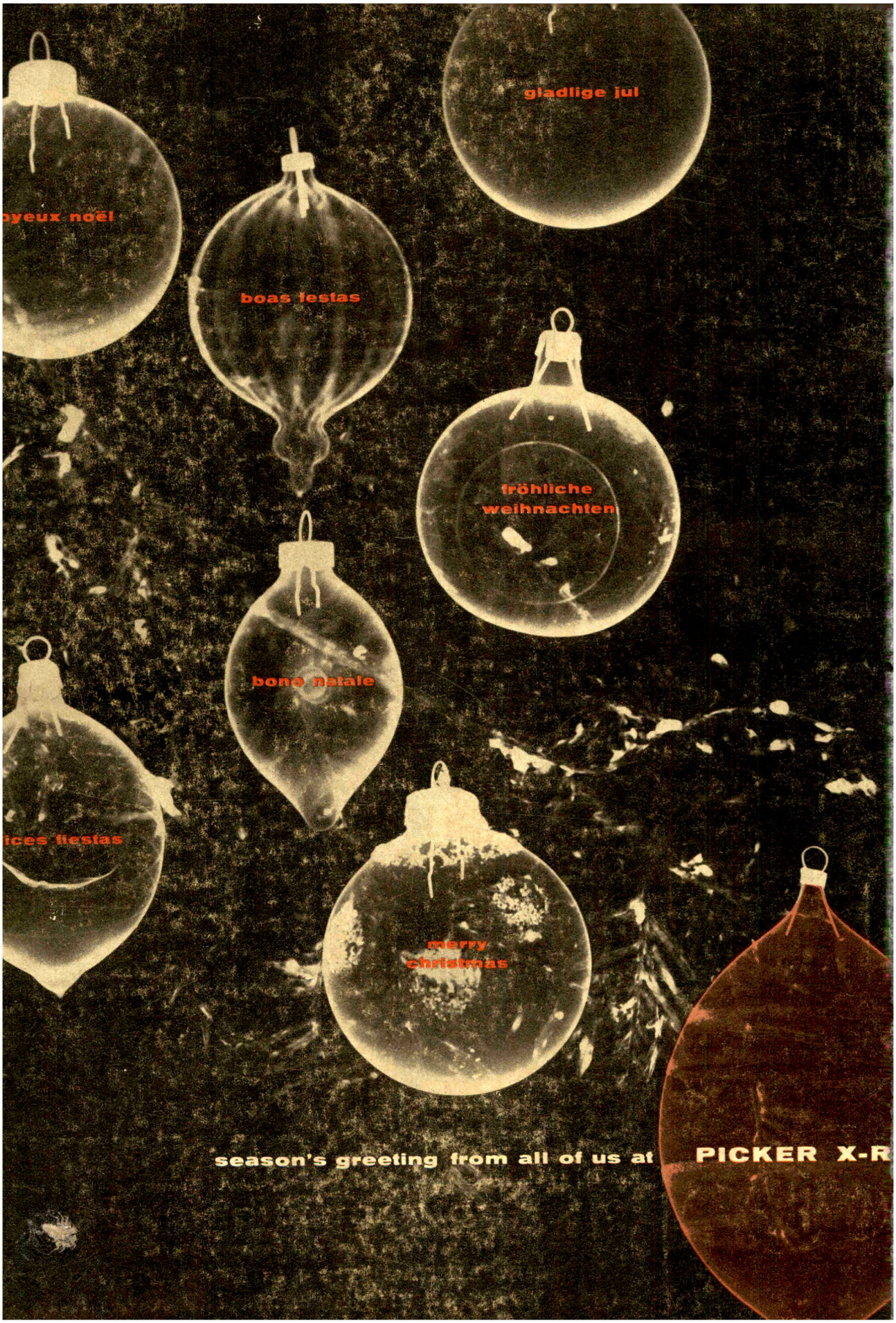
Reliability from experience with more than 250 particle accelerators in the field

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boas festas
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bono natale
ices fiestas
merry
christmas
season's greeting from all of us at PICKER X-R